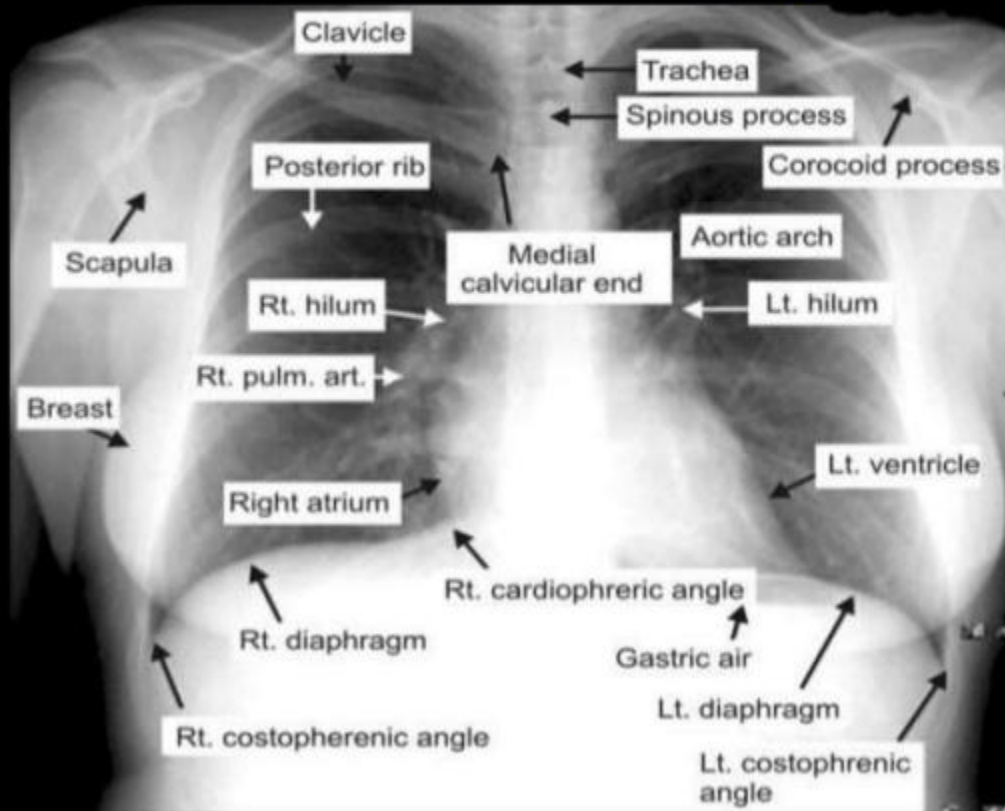


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Normal Anatomy



Respiratory physiology

Chloride shift

- CO₂ diffuses into RBCs
- CO₂ + H₂O $\xrightarrow{\text{carbonic anhydrase}}$ HCO₃⁻ + H⁺
- H⁺ combines with Hb
- HCO₃⁻ diffuses out of cell, Cl⁻ replaces it

Bohr Effect

- increasing acidity (or pCO₂) means O₂ binds less well to Hb

Haldane effect

- increase pO₂ means CO₂ binds less well to Hb

Control of respiration

- central regulatory centres
- central and peripheral chemoreceptors
- pulmonary receptors

Central regulatory centres:

- medullary respiratory centre
- apneustic centre (lower pons)
- pneumotaxic centre (upper pons)

Central and peripheral chemoreceptors:

- central: raised [H⁺] in ECF stimulates respiration
- peripheral: carotid + aortic bodies, respond to raised pCO₂ & [H⁺], lesser extent low pO₂

Pulmonary receptors:

- stretch receptors, lung distension causes slowing of respiratory rate (Hering-Breuer reflex)
- irritant receptor, leading to bronchoconstriction
- juxtacapillary receptors, stimulated by stretching of the microvasculature

Hypoxia

A fall in the partial pressure of oxygen pO₂ in the blood leads to vasoconstriction of the pulmonary arteries. → This allows blood to be diverted to better aerated areas of the lung and improves the efficiency of gaseous exchange

Pulmonary surfactant

- Surfactant is a mixture of phospholipids, carbohydrates and proteins released by type 2 pneumocytes.
- The main functioning component is dipalmitoyl phosphatidylcholine (DPPC) which reduces alveolar surface tension.
- first detectable around 28 weeks
- as alveoli decrease in size, surfactant concentration is increased, helping prevent the alveoli from collapsing
- reduces the muscular force needed to expand the lungs (i.e. decreases the work of breathing)

Pulmonary capillary wedge pressure (PCWP)

- Pulmonary capillary wedge pressure is measured using a balloon tipped Swan-Ganz catheter which is inserted into the pulmonary artery.
- The pressure measured is similar to that of the left atrium (normally 6-12 mmHg).
- One of the main uses of measuring the PCWP is determining whether pulmonary oedema is caused by either heart failure or ARDS.
- In many modern ITU departments PCWP measurement has been replaced by non-invasive techniques.

Lung compliance:

Defined as change in lung volume per unit change in airway pressure

Causes of increased compliance

- 1) age
- 2) emphysema - this is due to loss alveolar walls and associated elastic tissue

Causes of decreased compliance

- 1) pulmonary oedema
- 2) pulmonary fibrosis
- 3) pneumonectomy
- 4) kyphosis

Oxygen dissociation curve:

- The oxygen dissociation curve describes the relationship between the percentage of saturated haemoglobin and partial pressure of oxygen in the blood pO_2 .
- It is **not affected by haemoglobin** concentration
- **Shifts to left** = for given oxygen tension there is increased saturation of Hb with oxygen i.e. decreased oxygen delivery to tissues
- **Shifts to right** = for given oxygen tension there is reduced saturation of Hb with oxygen i.e. enhanced oxygen delivery to tissues

Shifts to L eft = L ower oxygen delivery	Shifts to R ight = R aised oxygen delivery
1) HbF, methaemoglobin, carboxyhaemoglobin 2) Low $[H^+]$ (alkali) 3) Low pCO_2 4) Low 2,3-DPG 5) Low temperature	1) Raised $[H^+]$ (acidic) 2) Raised pCO_2 3) Raised 2,3-DPG* 4) Raised temperature

The L rule:

Shifts to L → Lower oxygen delivery, caused by

- Low $[H^+]$ (alkali)
- Low pCO_2
- Low 2,3-DPG
- Low temperature

Another mnemonic is 'CADET, face Right!' for CO_2 , Acid, 2,3-DPG, Exercise and Temperature

*2,3-diphosphoglycerate

Carbon monoxide poisoning

- Carbon monoxide binds with haemoglobin with a greater affinity than oxygen displacing it from the blood causing tissue hypoxia.
- In addition carbon monoxide shifts the oxygen dissociation curve to the left reducing tissue delivery even more.

Symptoms of mild poisoning (carboxy haemoglobin levels = 10-30%)

- Headache, tiredness, nausea, dizziness and poor concentration.
- With increasing levels vomiting and weakness then impaired consciousness may occur with hypertension, tachycardia and flushing.

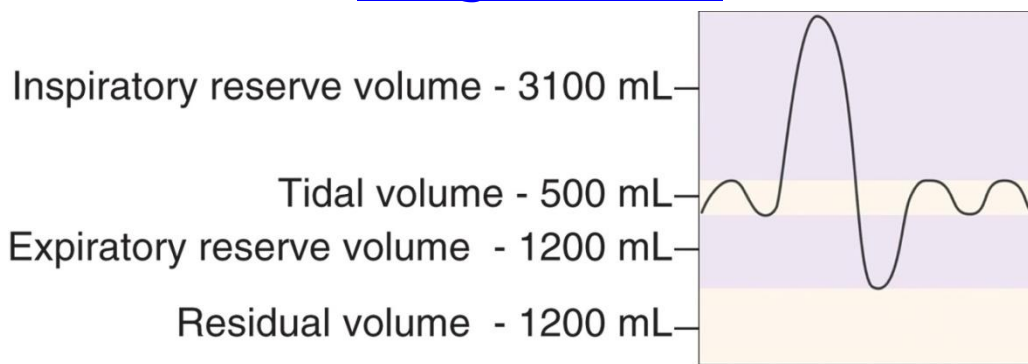
Severe poisoning (carboxy haemoglobin levels more than 50%)

- Convulsions, coma, respiratory depression and death can occur.

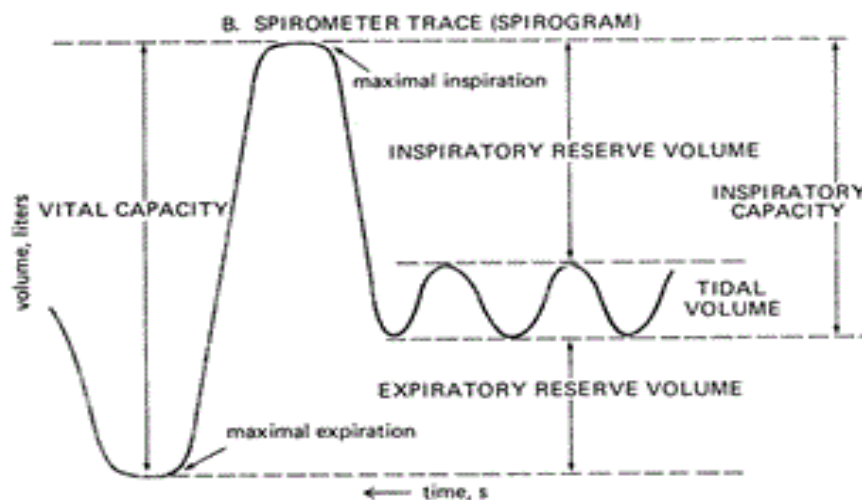
Treatment

- 1) 100% oxygen through a tight fitting, non-re-breathing face mask at a flow rate of 10 L/min.
- 2) In severe cases intubation and mechanical ventilation may be required and in these patients there is a place for hyperbaric oxygen.

Lung volumes



- 1) **Tidal volume (TV)**
 - volume inspired or expired with each breath at rest
 - 500ml in males, 350ml in females
- 2) **Inspiratory reserve volume (IRV) = 2-3 L**
 - maximum volume of air that can be inspired at the end of a normal tidal inspiration
 - inspiratory capacity = TV + IRV
- 3) **Expiratory reserve volume (ERV) = 750ml**
 - maximum volume of air that can be expired at the end of a normal tidal expiration
- 4) **Residual volume (RV) = 1.2L**
 - volume of air remaining after maximal expiration
 - increases with age
 - $RV = FRC - ERV$
- 5) **Vital capacity (VC)**
 - maximum volume of air that can be expired after a maximal inspiration
 - 4,500ml in males, 3,500 ml in females
 - decreases with age
 - $VC = \text{inspiratory capacity} + ERV$
- 6) **Total lung capacity (TLC)** is the sum of the vital capacity + residual volume
- 7) **Physiological dead space (V_D)**
 - $V_D = \text{tidal volume} * (PaCO_2 - PeCO_2) / PaCO_2$
 - where $PeCO_2$ = expired air CO_2



IRV-----Tidal volume (TV) -----ERV----- RV

مجموع الاثنين الاول من الشمال = IC

مجموع الثلاثة من الشمال = VC

مجموع الكل = TLC

FRC = functional residual capacity

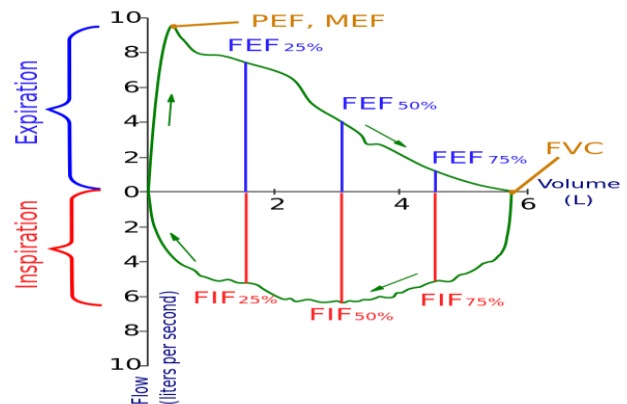
Pulmonary function tests

- Pulmonary function tests can be used to determine whether a respiratory disease is obstructive or restrictive.
- The table below summarises the main findings and gives some example conditions:

Obstructive lung disease	Restrictive lung disease
1) FVC : reduced or normal 2) FEV1 : significantly reduced 3) FEV1% (FEV1/FVC): reduced	1) FVC : significantly reduced 2) FEV1 : reduced 3) FEV1% (FEV1/FVC) - normal or increased
1) Asthma 2) COPD 3) Bronchiectasis 4) Bronchiolitis obliterans	1) Pulmonary fibrosis 2) Sarcoidosis (upper fibrosis) 3) Asbestosis (lower fibrosis) 4) Acute respiratory distress syndrome 5) Infant respiratory distress syndrome 6) Kyphoscoliosis 7) Neuromuscular disorders

Flow volume loop

- A normal flow volume loop is often described as a 'triangle on top of a semi circle'
- Flow volume loops are the most suitable way of assessing **compression of the upper airway**



Abbreviation	Name	Description
FVC	Forced Vital Capacity	This is the volume of air that can forcibly be blown out after full inspiration, measured in liters.
FEV₁	Forced Expiratory Volume in 1 Second	This is the maximum volume of air that can forcibly blow out in the first second during the FVC manoeuvre, measured in liters. Along with FVC it is considered one of the primary indicators of lung function.
FEV₁/FVC	FEV ₁ %	This is the ratio of FEV ₁ to FVC. In healthy adults this should be approximately 75–80%.
PEF	Peak Expiratory Flow	This is the maximal flow (or speed) achieved during the maximally forced expiration initiated at full inspiration, measured in liters per second.

Transfer factor

- The transfer factor describes the **rate** at which a **gas** will **diffuse** from **alveoli** into **blood**.
- Carbon monoxide is used to test the rate of diffusion.
- Results may be given as the total gas transfer (**TLCO**) or that corrected for lung volume (transfer coefficient, **KCO**)

Causes of a raised TLCO

- 1) asthma
- 2) pulmonary haemorrhage (Wegener's, Goodpasture's)
- 3) left-to-right cardiac shunts
- 4) polycythaemia
- 5) hyperkinetic states
- 6) male gender, exercise

Causes of a lower TLCO

- 1) COPD (much trapped air)
- 2) emphysema
- 3) pneumonia
- 4) pulmonary oedema
- 5) pulmonary fibrosis
- 6) pulmonary emboli
- 7) anaemia
- 8) low cardiac output

- KCO also tends to increase with age.

Some conditions may cause an increased KCO with a normal or reduced TLCO

- 1) Pneumonectomy/lobectomy
- 2) Diffuse pleural thickening (usually asbestos)
- 3) Scoliosis/kyphosis
- 4) Neuromuscular weakness
- 5) Ankylosis of costovertebral joints e.g. ankylosing spondylitis

Transfer factor

- **raised:** asthma, haemorrhage, left-to-right shunts, polycythaemia
- **low:** everything else

Where alveolar haemorrhage occurs the TLCO tends to increase due to the enhanced uptake of carbon monoxide by intra-alveolar haemoglobin

Chest x-ray

Cavitating lung lesion:

- 1) abscess (Staph aureus, Klebsiella and Pseudomonas)
- 2) Tuberculosis
- 3) Aspergillosis, histoplasmosis, coccidioidomycosis
- 4) Squamous cell lung cancer
- 5) Pulmonary embolism
- 6) Wegener's granulomatosis
- 7) Rheumatoid arthritis

Coin lesions:

- 1) Malignant tumour: lung cancer or metastases
- 2) Benign tumour: hamartoma
- 3) Infection: pneumonia, abscess, TB, hydatid cyst
- 4) AV malformation

Arterial blood gases

pH 7.35 - 7.45

pCO₂ 4.5 - 6.0 kPa

pO₂ 10 - 14 kPa

A 48-year-old male accountant is referred from his general practitioner with a three month history of dry, nocturnal cough. He is an ex-smoker having given up five years ago. He does not produce any sputum, has not suffered with any haemoptysis and despite his steady weight has an exercise tolerance similar to his work colleagues. He denies any other symptoms of note. Examination reveals he is 5' 10" (1.77m) tall and weighs 98kg (BMI = 31 kg/m²). Chest is clear to auscultation. Results of spirometry are shown below:

FEV ₁	3.0 L	(Predicted 3.38 L)
FVC	4.4 L	(Predicted 4.40 L)
FEV ₁ /FVC	0.68	(Predicted 0.77)
PEFR	540 L/min	(Predicted 559 L/min)

What would be the most appropriate first line investigation?

- a) 24 Hour oesophageal pH and manometry
- b) Bronchoscopy
- c) Flexible nasendoscopy
- d) Peak flow chart This is the correct answer
- e) Sleep studies

Three common causes to consider with nocturnal dry cough are: asthma, reflux and post nasal drip.

The clue here is the obstructive picture on spirometry (FEV₁/FVC ratio <70%) - which immediately excludes reflux and post nasal drip (there is no reason for these conditions to have abnormal presentation on spirometry). Effectively excluding oesophageal manometry and nasendoscopy from the options available. If this were a case of obstructive sleep apnoea, one would expect a restrictive defect secondary to obesity, hence excluding sleep studies as a useful entity.

Bronchoscopy looking for a bronchial carcinoma for instance which may also present with an obstructive defect, is a viable option but there is nothing in the history which points to a diagnosis of malignancy in this man and as a first line investigation bronchoscopy compared to maintaining a peak flow chart is an highly invasive investigation.

A variation of greater than 25% on a peak flow chart (pre and post bronchodilator) would support an initial diagnosis of reversible small airways disease, such as asthma.

Asthma

Diagnosis:

- Whilst the diagnosis of asthma remains largely clinical, the British Thoracic Society (BTS) guidelines do offer some guidance on how we should approach this problem, for both adults and children.
- They recommend we classify patients as having either a high, intermediate or low probability of asthma based on the presence or absence of certain symptoms
- For adults it is recommend that they have a clinical assessment including **spirometry** (or **Peak Expiratory Flow** measurement if spirometry is not available)
- When assessing patients we should therefore look for symptoms which may support a diagnosis of asthma, and those which may point to an alternative diagnosis.
- The BTS produced **a list of features** which are helpful when deciding this:

Features which make a diagnosis of asthma more likely	Features which make a diagnosis of asthma less likely
1) More than one of the following symptoms: wheeze, breathlessness, chest tightness and cough particularly if: ⇒ symptoms worse at night and in the early morning ⇒ symptoms in response to exercise, allergen exposure and cold air ⇒ symptoms after taking aspirin or beta blockers 2) History of atopic disorder 3) Family history of asthma and/or atopic disorder 4) Widespread wheeze heard on auscultation of the chest 5) Otherwise unexplained low FEV1 or PEF (historical or serial readings) 6) Otherwise unexplained peripheral blood eosinophilia	1) Prominent dizziness, light-headedness, peripheral tingling 2) Chronic productive cough in the absence of wheeze or breathlessness 3) Voice disturbance 4) Symptoms with colds only 5) Significant smoking history (i.e. > 20 pack-years) 6) Cardiac disease 7) Repeatedly normal physical examination of chest when symptomatic 8) Normal PEF or spirometry when symptomatic

High probability:

- If a patient has many symptoms which make a diagnosis of asthma more likely
- Then the BTS recommend that we **start a trial of treatment**.
 - ⇒ **A good response** is considered a **positive 'test of reversibility'**.
 - ⇒ If **poor response** to treatment then **further investigations** should be considered.

Low probability:

- For patients with a low probability of asthma then an alternative diagnosis should be sought.
- Further investigations and referral to a respiratory specialist considered.

Intermediate probability:

- If a patient has an intermediate probability of asthma the BTS recommend 'to carry out further investigations, including an explicit trial of treatments for a specified period, before confirming a diagnosis and establishing maintenance treatment. '.
 - The accompanying algorithm suggests this decision should be partly guided by the FEV₁/FVC ratio - a ratio of < 0.7 is suggestive of asthma. (normal 0.75-0.8)
- ☒ It should of course be noted that spirometry may be normal in asymptomatic patients so it may be necessary to repeat spirometry or peak flow readings on a number of occasions in patients where the diagnosis is not clear.
- ☒ It is now recognised that in patients with normal or near-normal pre-treatment lung function there is little room for measurable improvement in FEV₁ or peak flow.
- ☒ > 400 ml improvement in FEV₁ is considered significant after 400 mcg inhaled salbutamol
- ☒ in patients with diagnostic uncertainty and airflow obstruction present at the time of assessment if there is an incomplete response to inhaled salbutamol, give either inhaled corticosteroids (200 mcg twice daily beclometasone equivalent for 6-8 weeks) or oral prednisolone (30 mg OD for 14 days) ????

It is now advised to interpret peak flow variability with caution due to the poor sensitivity of the test

- diurnal variation % = [(Highest - Lowest PEFr) / Highest PEFr] x 100
- assessment should be made over 2 weeks
- > 20% diurnal variation is considered significant

What is the most appropriate initial treatment?

The BTS state the following:

- 1) Patients should start treatment at the step most appropriate to the initial severity of their asthma
⇒ This means that for some patients prescribing a corticosteroid inhaler in addition to a salbutamol inhaler is appropriate.
- 2) The BTS suggest the following patients would benefit from a corticosteroid inhaler: (Inhaled steroids should be considered for patients with any of the following asthma-related features):
 - 1) exacerbations of asthma in the last 2 years
 - 2) using inhaled β₂ agonists 3 times a week or more
 - 3) symptomatic 3 times a week or more
 - 4) waking one night a week

The last two points are probably the most relevant to newly diagnosed patients.

Asthma: stepwise management in adults

The management of stable asthma is now well established with a step-wise approach:

Step	Management
Step 1	Inhaled short-acting B2 agonist as required
Step 2	Add inhaled steroid at 200-800 mcg/day* 400 mcg is an appropriate starting dose for many patients. Start at dose of inhaled steroid appropriate to severity of disease
Step 3	1. Add inhaled long-acting B2 agonist (LABA) 2. Assess control of asthma: ☒ good response to LABA → continue LABA ☒ benefit from LABA but control still inadequate : ⇒ continue LABA and ⇒ increase inhaled steroid dose to 800 mcg/day* (if not already on this dose) ☒ no response to LABA: ⇒ stop LABA and ⇒ Increase inhaled steroid to 800 mcg/ day.* ⇒ If control still inadequate, institute trial of other therapies , → leukotriene receptor antagonist or SR theophylline
Step 4	Consider trials of: 1) increasing inhaled steroid up to 2000 mcg/day* 2) Addition of a fourth drug e.g. ☒ Leukotriene receptor antagonist , ☒ SR theophylline , ☒ B2 agonist tablet The BTS say there is little evidence to separate the different options available. They do however suggest that leukotriene receptor antagonists are least likely to cause side-effects. Monitoring of serum concentrations may also be required for theophyllines
Step 5	1) Use daily steroid tablet in lowest dose providing adequate control. Consider other treatments to minimize the use of steroid tablets 2) Maintain high dose inhaled steroid at 2000 mcg/day* 3) Refer patient for specialist care

*beclometasone dipropionate or equivalent

Additional notes

- A) **Leukotriene receptor antagonists:** e.g. Montelukast, zafirlukast
- 1) have both anti-inflammatory and bronchodilatory properties
 - 2) should be used when patients are poorly controlled on high-dose inhaled corticosteroids and a long-acting b2-agonist
 - 3) Leukotriene antagonists are licensed for use in asthma with **allergic rhinitis** and have been shown to be as effective as doubling the dose of inhaled steroid.
 - 4) They are also particularly useful in **exercise-induced asthma** and **adult onset aspirin sensitive asthma**.
 - 5) associated with the development of **Churg-Strauss syndrome**
- B) **Fluticasone** is more lipophilic and has a longer duration of action than beclometasone
- C) **Hydrofluoroalkane** is now replacing chlorofluorocarbon as **the propellant of choice**. Only half the usually dose is needed with hydrofluoroalkane due to the smaller size of the particles
- D) **Long acting B2-agonists**
- Acts as bronchodilators but also inhibit mediator release from mast cells.
 - Recent meta-analysis showed adding salmeterol improved symptoms compared to doubling the inhaled steroid dose

Acute severe Asthma

Patients with acute severe asthma are stratified into moderate, severe or life-threatening

Moderate	Severe	Life-threatening
1) PEFR 50-75% best or predicted	1) PEFR 33 - 50% best or predicted	1) PEFR < 33% best or predicted
2) Speech normal	2) Can't complete sentences	2) O2 sats < 92%, PO2 <8(60), normal PCO2
3) RR < 25 / min	3) RR > 25/min	3) Silent chest, cyanosis or feeble respiratory effort
4) Pulse < 110 bpm	4) Pulse > 110 bpm	4) Bradycardia, dysrhythmia or hypotension
		5) Exhaustion, confusion or coma

Note that a patient having any one of the life-threatening features should be treated as having a life-threatening attack.

British Thoracic Society guidelines:

- 1) **Magnesium sulphate** recommended as next step for patients who are not responding (e.g. 1.2 - 2g IV over 20 mins)
 - 2) little evidence to support use of **IV aminophylline** (although still mentioned in management plans)
 - 3) If no response consider **IV salbutamol**
 - 4) Hypercapnia and signs of fatigue are indications for **immediate intubation and ventilation**.
 - 5) Non-invasive ventilation is not recommended in acute severe asthma.
- ☒ The British Thoracic Society defines **near fatal asthma** as an attack with **raised PaCO₂** and/or requiring mechanical ventilation with raised inflation pressures.

Occupational Asthma

(10% of adult asthma)

- The symptoms do not usually develop immediately on first exposure but begin days, months or even years later.
- Patients may either present with concerns that chemicals at work are worsening their asthma or you may notice in the history that symptoms seem better at weekends / when away from work
وممكن كان كويس فى الشغل لما يسافر اجازة ويرجع يتدهور
- Exposure to the following chemicals is associated with occupational asthma:
 - 1) **Isocyanates:**
 - ✓ The most common cause.
 - ✓ Example occupations include spray painting and foam moulding using adhesives
 - 2) Platinum salts
 - 3) Soldering flux resin
 - 4) Glutaraldehyde
 - 5) Epoxy resins
 - 6) Proteolytic enzymes
 - 7) Bakers (flour mainly but also enzymes such as amylase used in the baking process)
 - 8) Chemical processors (acids, detergents, bleaches)
 - 9) Plastics workers (polyethylene, polyvinyl chloride)
 - 10) Solderers (colophony), and
 - 11) Laboratory technicians (rats, mice, rabbits, locusts).
- Serial measurements of **peak expiratory flow** are recommended at work and away from work.
- Referral should be made to a respiratory specialist for patients with suspected occupational asthma.
- Removal from exposure to the sensitizing agent at an early stage can lead to remission of asthma although sensitisation to the agent is usually permanent.

Assessing a patient's **performance status** is important when evaluating the most appropriate treatment options. It is commonly used by cancer MDTs, but has a role in assessing patients with chronic illnesses including COPD.

WHO Scale	Description
0	Asymptomatic
1	Symptomatic but ambulatory (can carry out light work)
2	In bed <50% of the day. Unable to work but can live at home with some assistance
3	In bed >50% of the day but unable to care for self
4	Bedridden

Medical Research Council dyspnoea scale:

Grade	Degree of breathlessness related to activities
1	Not troubled by breathlessness except on strenuous exercise
2	Short of breath when hurrying or walking up a slight hill
3	Walks slower than contemporaries on level ground because of breathlessness, or has to stop for breath when walking at own pace
4	Stops for breath after walking about 100 m or after a few minutes on level ground
5	Too breathless to leave the house, or breathless when dressing or undressing

Theophylline

- Theophylline, like caffeine, is one of the naturally occurring **methylxanthines**.
- The main use of theophyllines in clinical medicine is as a bronchodilator in the management of asthma and COPD
- The exact mechanism of action has yet to be discovered.
- One theory suggests theophyllines may be:
 - **Non-specific phosphodiesterase inhibitor** resulting in an increase in cAMP or
 - **Antagonism of adenosine** and
 - **Prostaglandin inhibition**

Theophylline poisoning

Features:

- 1) Acidosis, hypokalaemia, hypoPh, hypoMg, hypoNa
- 2) hyperglycemia & hyperCa
- 3) vomiting
- 4) tachycardia, arrhythmias, tremors
- 5) seizures

Management:

- 1) activated charcoal
- 2) charcoal haemoperfusion is preferable to haemodialysis

Factors **decreasing** theophylline **clearance**:

- ☒ Disease:
 - 1) Hepatic cirrhosis
 - 2) Congestive cardiac failure
 - 3) COPD,
 - 4) Acute febrile illnesses, Pneumonia,
 - 5) Acute pulmonary oedema,
- ☒ Drugs: Cimetidine, Oral contraceptive pill, Erythromycin, Ciprofloxacin
- ☒ Diet: High carbohydrate intake, High methylxanthine intake (tea, coffee)
- ☒ Obesity

Factors **increasing** theophylline **clearance**:

- ☒ Diet: Low carbohydrate, High protein intake
- ☒ Cigarette smoking
- ☒ Drugs: Rifampicin, Carbamazepine.

COPD

Causes:

- 1) Smoking
- 2) Alpha-1 antitrypsin deficiency

Other causes: 4 C+ grain

- 1) cadmium (used in smelting)
- 2) coal
- 3) cotton
- 4) cement
- 5) grain

Diagnosis:

- 1) NICE recommend considering a diagnosis of COPD in patients over 35 years of age who are **smokers** or **ex-smokers** and **have symptoms** such as exertional breathlessness, chronic cough or regular sputum production.
- 2) The following investigations are recommended in patients with suspected COPD:
 - A. post-bronchodilator spirometry to demonstrate airflow obstruction:
⇒ **FEV1/FVC ratio less than 70%** (normal 75- 80%)
 - B. Chest x-ray:
⇒ Hyperinflation, bullae, flat hemidiaphragm.
⇒ Also important to exclude lung cancer
 - C. full blood count: exclude secondary polycythaemia
 - D. body mass index (BMI) calculation

- The **severity of COPD** is categorized using the FEV1*:

Post-bronchodilator FEV1/FVC	FEV1 (of predicted)	Severity
< 0.7	> 80%	Stage 1 - Mild**
< 0.7	50-79%	Stage 2 - Moderate
< 0.7	30-49%	Stage 3 - Severe
< 0.7	< 30%	Stage 4 - Very severe

Measuring **peak expiratory flow** is of limited value in COPD, as it may underestimate the degree of airflow obstruction.

*note that the grading system has changed following the 2010 NICE guidelines. If the FEV1 is greater than 80% predicted but the post-bronchodilator FEV1/FVC is < 0.7 then this is classified as Stage 1 - mild

**symptoms should be present to diagnose COPD in these patients

Management of stable COPD:

NICE updated its guidelines on the management of chronic obstructive pulmonary disease (COPD) in 2010.

General management:

- 1) smoking cessation advice
- 2) annual influenza vaccination
- 3) one-off pneumococcal vaccination

Bronchodilator therapy:

A) a short-acting beta2-agonist (SABA) or short-acting muscarinic antagonist (SAMA) is **first-line treatment**

B) for patients who remain breathless or have exacerbations despite using short-acting bronchodilators the next step is determined by the FEV1:

FEV1 > 50% (Mild & Moderate COPD)

- long-acting beta2-agonist (LABA), for example **salmeterol** or
- long-acting muscarinic antagonist (LAMA), for example **tiotropium**

FEV1 < 50 % (Severe & Very severe COPD)

- LABA + inhaled corticosteroid (ICS) in a combination inhaler or
- LAMA

C) For patients with persistent exacerbations or breathlessness

- if taking a LABA then switch to a LABA + ICS combination inhaler
- otherwise give a LAMA and a LABA + ICS combination inhaler

Reason for using inhaled corticosteroids – To reduce exacerbations

Oral theophylline:

- NICE only recommends theophylline after trials of short and long-acting bronchodilators or to people who cannot use inhaled therapy
- the dose should be reduced if macrolide or fluoroquinolone antibiotics are co-prescribed

Mucolytics:

Should be considered in patients with a chronic productive cough and continued if symptoms improve

Factors which may improve survival in patients with stable COPD:

- 1) smoking cessation - the **single most important** intervention in patients who are still smoking
- 2) long term oxygen therapy (LTOT) in patients who fit criteria
- 3) lung volume reduction surgery in selected patients

Management of acute COPD exacerbations:

- A) **The most common bacterial organisms** that cause infective exacerbations of COPD are:
- 1) Haemophilus influenza (most common cause)
 - 2) Streptococcus pneumoniae
 - 3) Moraxella catarrhalis
- B) **Respiratory viruses account for around 30% of exacerbations**, with the **human rhinovirus** being the most important pathogen.

NICE guidelines from 2010 recommend the following:

- 1) **Increase frequency of bronchodilator** use and consider giving via a **nebulizer**
- 2) Give **prednisolone 30 mg daily for 7-14 days**
- 3) It is common practice for all patients with an exacerbation of COPD to receive **antibiotics**. NICE do not support this approach. They recommend giving **oral antibiotics** 'if sputum is purulent or there are clinical signs of pneumonia'

Long-term oxygen therapy in COPD

- The 2010 NICE guidelines on long-term oxygen therapy (LTOT) in COPD.
- Patients who receive LTOT should breathe supplementary oxygen for **at least 15 hours/day**.
- **Oxygen concentrators** are used to provide a fixed supply for LTOT.
- **Assess patients if any of the following:**
 - 1) Very severe airflow obstruction ($FEV_1 < 30\%$ predicted).
Assessment should be 'considered' for patients with severe airflow obstruction ($FEV_1 30-49\%$ predicted)
 - 2) cyanosis
 - 3) oxygen saturations less than or equal to 92% on room air
 - 4) polycythaemia
 - 5) peripheral oedema
 - 6) raised jugular venous pressure
- **Assessment is done by measuring ABG on 2 occasions at least 3 weeks apart in patients with stable COPD on optimal management.**
- **Offer LTOT to patients with:**
 - ⇒ **$PO_2 < 7.3$ (55)** or to
 - ⇒ Those with a **pO_2 of 7.3 - 8 (55-60)** and one of the following:
 - 1) Secondary polycythaemia
 - 2) Nocturnal hypoxemia
 - 3) Peripheral oedema
 - 4) Pulmonary hypertension

LTOT and smoking cessation are currently the only interventions in COPD that have been shown to prolong life.

Cor pulmonale

Features:

- 1) peripheral oedema,
 - 2) raised jugular venous pressure,
 - 3) systolic parasternal heave,
 - 4) loud P2
- use a **loop diuretic** for oedema, consider **long-term oxygen therapy**
 - ~~ACE inhibitors, calcium channel blockers and alpha blockers~~ are **not recommended** by NICE

Alpha-1 antitrypsin deficiency

- A common inherited condition caused by a **lack of a protease inhibitor (Pi)** normally produced by the liver.
- The role of A1AT is to protect cells from enzymes such as neutrophil elastase.

Genetics:

- 1) located on **chromosome 14**
- 2) inherited in an **autosomal recessive / co-dominant fashion***
- 3) alleles classified by their electrophoretic mobility: M for normal, S for slow, and Z for very slow:
 - ⇒ normal = PiMM
 - ⇒ homozygous PiSS (50% normal A1AT levels)
 - ⇒ homozygous PiZZ (10% normal A1AT levels)

Features:

Patients who manifest disease usually have **PiZZ genotype**

- 1) **panacinar emphysema**, most marked in lower lobes
- 2) liver:
 - **cholestasis** in **children**
 - **cirrhosis** and **hepatocellular carcinoma** in **adults**,

Investigations:

- A1AT concentrations

Management:

- 1) no smoking
- 2) supportive: **bronchodilators**, **physiotherapy**
- 3) intravenous **alpha1-antitrypsin protein concentrates**
- 4) surgery:
 - ✓ volume reduction surgery,
 - ✓ **lung transplantation**

*trusted sources are split on which is a more accurate description

Obstructive sleep apnoea/hypopnoea syndrome

- Obstructive sleep apnoea/hypopnoea syndrome occurs when episodes of partial or complete obstruction of the pharyngeal airway occur during sleep.
- This causes
 - Repetative apnoeas (cessation of airflow for more than 10 seconds) and hypopnoeas (50% reduction in airflow for greater than 10 seconds)
 - Loud snoring and
 - Excessive daytime somnolence as a result of repeated arousals.

Predisposing factors:

- 1) **Obesity**
- 2) Macroglossia: **acromegaly, hypothyroidism, amyloidosis**
- 3) Large tonsils
- 4) **Marfan's syndrome**

Consequence:

- **daytime somnolence**
- **hypertension**

SIGN guidelines for the diagnosis and management of patients with OSAHS were published in 2003

Assessment of sleepiness:

- 1) **Epworth Sleepiness Scale** - questionnaire completed by patient +/- partner
- 2) **Multiple Sleep Latency Test (MSLT)** - measures the time to fall asleep in a dark room (using EEG criteria)

Diagnostic tests:

Sleep studies:

Ranging from:

- ⇒ monitoring of pulse oximetry at night to
- ⇒ full polysomnography where a wide variety of physiological factors are measured including EEG, respiratory airflow, thoraco-abdominal movement, snoring and pulse oximetry

Management:

- 1) weight loss, avoid alcohol excess & sedatives
- 2) **Nasal CPAP** is **first line** for moderate or severe OSAHS
- 3) intra-oral devices (e.g. mandibular advancement) may be used if CPAP is not tolerated or for patients with mild OSAHS where there is no daytime sleepiness
- 4) limited evidence to support use of pharmacological agents

The severity of obstructive sleep apnoea/hypopnoea syndrome is dependent on the patient's symptoms but generally an apnoea/ hypopnoea index (AHI):

- ⇒ 4-14 mild
- ⇒ 15-30 moderate
- ⇒ >30 severe.

DVLA must be involved.

Bronchiectasis

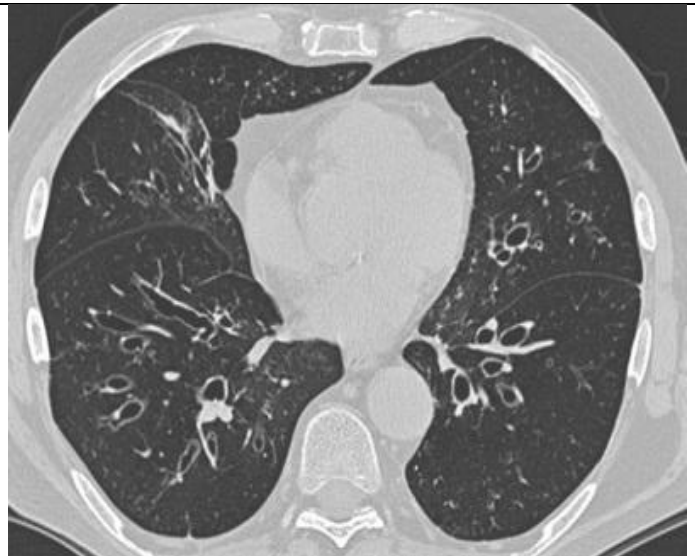
- Bronchiectasis describes a **permanent dilatation of the airways secondary to chronic infection or inflammation.**
- There are a wide variety of causes are listed below:

Causes:

- 1) post-infective: **tuberculosis, measles, pertussis, pneumonia**
- 2) allergic bronchopulmonary aspergillosis (**ABPA**)
- 3) immune deficiency: **selective IgA, hypogammaglobulinaemia**
- 4) bronchial obstruction e.g. **lung cancer/foreign body**
- 5) cystic fibrosis
- 6) Ciliary dysketic syndromes: **Kartagener's syndrome, Young's syndrome**
- 7) yellow nail syndrome (**lymphoedema, pleural effusion & yellow nail**)



Chest x-ray showing tramlines, most prominent in the left lower zone



CT chest showing widespread tram-track and signet ring signs

Management:

After assessing for treatable causes (e.g. immune deficiency) management is as follows:

- 1) physical training (e.g. inspiratory muscle training) - has a good evidence base for patients with non-cystic fibrosis bronchiectasis
- 2) postural drainage
- 3) antibiotics for exacerbations + long-term rotating antibiotics in severe cases
- 4) bronchodilators in selected cases
- 5) immunizations
- 6) surgery in selected cases (e.g. Localised disease)

Most common organisms isolated from patients with bronchiectasis:

- 1) **Haemophilus influenza** (most common)
- 2) **Pseudomonas aeruginosa**
- 3) **Klebsiella spp.**
- 4) **Streptococcus pneumoniae**

Cystic fibrosis

Autosomal Recessive (mucoviscidosis)

Presenting features:

- 1) Neonatal period (around 20%):
 - ✓ meconium ileus,
 - ✓ less commonly prolonged jaundice
- 2) Recurrent chest infections (40%) (**pseudomonas**)
- 3) malabsorption (30%): **steatorrhea, failure to thrive**
- 4) **Other features** (10%):
 - 1) Liver disease
 - 1) Short stature
 - 2) Delayed puberty
 - 3) Diabetes mellitus
 - 4) Rectal prolapse (due to bulky stools)
 - 5) Nasal polyps
 - 6) Male infertility (as the vas deferens fails to develop).
 - 7) Female subfertility

Diagnosis:

- 1) **Sweat test:**

Patients with CF have abnormally high **sweat chloride & sodium**

 - ⇒ normal value < 40 mEq/l,
 - ⇒ CF indicated by > 60 mEq/l
- 2) The diagnosis is usually confirmed by determining **the patient's genotype**.

Causes of false positive sweat test:

- 1) Malnutrition
- 2) Glycogen storage diseases
- 3) G6PD
- 4) Adrenal insufficiency
- 5) Nephrogenic diabetes insipidus
- 6) Hypothyroidism, hypoparathyroidism
- 7) Ectodermal dysplasia

Management:

Management of cystic fibrosis involves a multidisciplinary approach

Key points:

- 1) Regular (at least twice daily) **chest physiotherapy** and **postural drainage**. Parents are usually taught to do this. Deep breathing exercises are also useful
- 2) **High calorie diet**, including **high fat intake***.....العيان الوحيد الى تقوله كل دهون
- 3) **Pancreatic enzyme supplements** taken with meals & **vitamin supplementation**
- 4) **Heart and lung transplant**

*this is now the standard recommendation - previously high calorie, low-fat diets have been recommended to reduce the amount of steatorrhea

Kartagener's syndrome

- Also known as **primary ciliary dyskinesia**
- First described in 1933
- Most frequently occurs in examinations due to its association with **dextrocardia** (e.g. 'quiet heart sounds', 'small volume complexes in lateral leads')

Features:

- 1) dextrocardia or complete situs inversus
- 2) bronchiectasis
- 3) recurrent sinusitis
- 4) subfertility (secondary to diminished sperm motility and defective ciliary action in the fallopian tubes)

Yellow nail syndrome

- Caused by **hypoplastic lymphatics** and is characterised by the triad of:
 - 1) Lymphoedema
 - 2) Pleural effusions, and
 - 3) Yellow discolouration of the nails.
- Approximately 40% of patients also have **bronchiectasis**.





The culture plate shows a growth of *Pseudomonas aeruginosa*, characterised by the green colouration of the colonies - due to production of the pigment pyocyanin.

ARDS

Caused by increased permeability of alveolar capillaries leading to fluid accumulation in alveoli i.e. **non-cardiogenic pulmonary oedema**

Criteria (American-European Consensus Conference)

- 1) acute onset
- 2) bilateral infiltrates on CXR
- 3) non-cardiogenic (pulmonary artery wedge pressure needed if doubt)
(**PAWP <18 mmHg**)
- 4) $PO_2/FiO_2 < 200$ mmHg ($PaO_2:FiO_2$ ratio of less than 26.7 kPa)

Causes:

- 1) infection: sepsis, pneumonia
- 2) massive blood transfusion
- 3) trauma
- 4) smoke inhalation
- 5) pancreatitis
- 6) cardio-pulmonary bypass

ARDS in sepsis

- ARDS is a common complication of severe sepsis.
- The ARDS net guidelines feature prominently in the Surviving Sepsis guidelines, with a special emphasis on factors that are important in severe sepsis.
- The target tidal volume is based on ideal, rather than actual body weight. Fat has no alveoli
- A target tidal volume of **6 ml/kg** ideal body weight should be set maintaining plateau pressures of less than 30 cmH₂O.
- **A high-PEEP** strategy is recommended to reduce atelecto-trauma.
- Turning the patient prone and recruitment manoeuvres are recommended for worsening hypoxaemia.
- Pulmonary artery catheters should not be used routinely and a conservative fluid strategy should be used where possible.
- Non-invasive ventilation (NIV) should not be routinely used and only in carefully considered in a minority of cases.

Community-acquired Pneumonia

CAP may be caused by the following infectious agents:

- 1) Streptococcus pneumoniae (accounts for around 80% of cases)
- 2) Haemophilus influenza
- 3) Staphylococcus aureus: commonly after the 'flu
- 4) Atypical pneumonias (e.g. Due to Mycoplasma pneumoniae)
- 5) Viruses
- 6) Klebsiella pneumoniae is classically in alcoholics

Streptococcus pneumoniae (pneumococcus)

- The most common cause of community-acquired pneumonia
- Characteristic features of pneumococcal pneumonia:
 - 1) Rapid onset
 - 2) High fever
 - 3) Pleuritic chest pain, herpes labialis

Pneumonia prognostic factors: CURB-65 criteria of severe pneumonia

- 1) Confusion (abbreviated mental test score $\leq 8/10$)
- 2) Urea > 7 mmol/L
- 3) Respiratory rate ≥ 30 / min
- 4) BP: systolic ≤ 90 or diastolic ≤ 60 mmHg
- 5) Age ≥ 65 years

- Low severity: ----- CURB-65 0-1 ----- mortality $<3\%$
- Moderate severity: ---- CURB-65 2 ----- mortality 9%
- High severity: ----- CURB-65 3-5, ----- mortality 15-40%

Other factors associated with a poor prognosis include:

- 1) Presence of coexisting disease
- 2) Hypoxemia ($pO_2 < 8 = 60$) independent of FiO_2
- 3) Temperature less than $35^\circ C$ or more than $40^\circ C$.
- 4) WBC less than $4 \times 10^9/L$ or greater than $20 \times 10^9/L$
- 5) Multi-lobar involvement on CXR

Management: The British Thoracic Society published guidelines in 2009:

Low Severity CAP: → Oral amoxicillin alone whether treated at home or in hospital.

Moderate CAP: → amoxicillin + clarithromycin

- ☒ If the oral route is not possible, benzylpenicillin and clarithromycin should be used.
- ☒ Doxycycline may be used as an alternative antibiotic regime, but is not the preferred treatment

High severity CAP:

- 1) IV co-amoxiclav + clarithromycin OR
- 2) cefuroxime (Zinacef) + clarithromycin OR
- 3) cefotaxime (claforan) + clarithromycin

The current BNF has slightly different recommendations مش مهمه

A) for high severity CAP:

- 1) Intravenous Benzylpenicillin + clarithromycin OR
- 2) Intravenous Benzylpenicillin + doxycycline.

B) For 'life-threatening' infections the same as BTS guidelines for high-severity CAP

Mycoplasma pneumoniae

- Mycoplasma pneumoniae is a cause of **atypical pneumonia**
- Often affects younger patients (**15-30 yrs**).
- It is associated with a number of characteristic complications such as:
 - 1) **erythema multiforme** and
 - 2) **Cold autoimmune haemolytic anaemia**.
- Epidemics of Mycoplasma pneumoniae classically occur every **4 years**.
- It is important to recognise atypical pneumonias as they may not respond **to penicillins** or **cephalosporins** due to it lacking a **peptidoglycan** cell wall.

Features:

- 1) the disease typically has a prolonged and gradual onset
- 2) flu-like symptoms classically precede a dry cough
- 3) bilateral consolidation on x-ray
- 4) Complications:(10%)
 - 1) cold agglutins (IgM) may cause an haemolytic anaemia, thrombocytopenia
 - 2) erythema multiforme, erythema nodosum
 - 3) meningoencephalitis, meningism,
 - 4) Guillain-Barre syndrome
 - 5) bullous myringitis: painful vesicles on the tympanic membrane
 - 6) pericarditis/myocarditis
 - 7) hepatitis, pancreatitis
 - 8) acute glomerulonephritis

Investigations:

- 1) diagnosis is generally by Mycoplasma serology
Diagnosis is based on demonstration of anti-mycoplasma antibodies in paired sera.
- 2) positive cold agglutination test

Management:

- 1) First choice treatment is with **macrolide antibiotic** (**erythromycin/clarithromycin**)
- 2) tetracyclines such as **doxycycline** are an alternative

Hospital-acquired pneumonia	✗ Within 5 days of admission: co-amoxiclav or cefuroxime ✗ >5 days after admission: ⇒ piperacillin with tazobactam OR ⇒ a broad-spectrum cephalosporin (e.g. ceftazidime) OR ⇒ a quinolone (e.g. ciprofloxacin)
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Aspiration pneumonia

- The most frequent conditions associated with aspiration pneumonia are decreased consciousness and dysphagia.

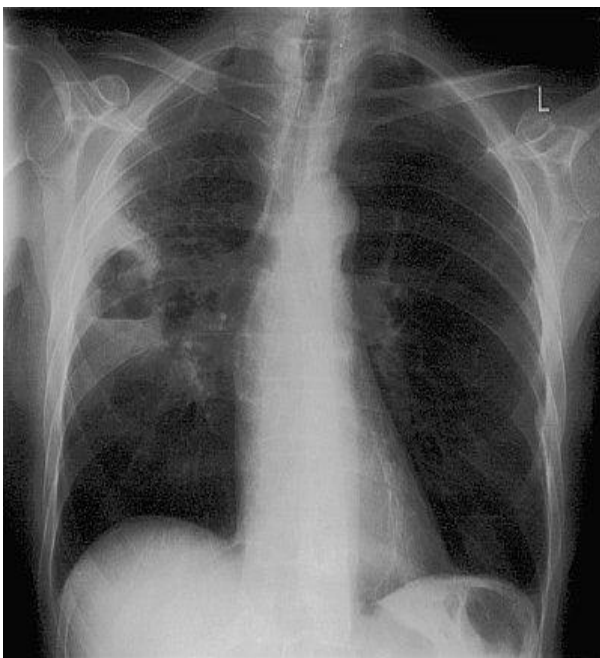
Risk factors for impaired consciousness:

- Epilepsy
- High alcohol intake and
- Use of recreational drugs with a history of drug overdose.
- Dental sepsis also increases the risk by increasing the anaerobic flora in the mouth and pharynx.
- Infection, particularly in the community, usually results from anaerobic organisms such as *Peptostreptococcus* and *Bacteroides*.
- Anaerobic infection can result in pneumonia, lung abscesses and empyema.
- Aspiration pneumonia can be indistinguishable from bacterial community acquired pneumonia in the early stages, as foul smelling sputum does is not usually present until necrosis has occurred.
- The dependent segments of the lung are usually involved, that is, the posterior segments of the upper lobes and apical segments of the lower lobes when the patient is supine and the lower lobes when the patient is upright.

Treatment:

☒ amoxicillin and metronidazole

- Monotherapy would be insufficient in a case of aspiration pneumonia.
 - The amoxicillin is used primarily to cover aerobes and facultative aerobes, and
 - the metronidazole targets anaerobes
 - They are required in conjunction to offer optimal cover.
- ☒ In cases of serious side effects, the regime would need to be re-considered**



The slide shows an abscess in the right mid-zone.

Legionella

- Legionnaire's disease is caused by the **intracellular bacterium Legionella pneumophila**.
- Gram negative rod
- It typically colonizes water tanks and hence questions may hint at air-conditioning systems or foreign holidays.
- Person-to-person transmission is not seen

Features:

- 1) flu-like symptoms including fever (present in > 95% of patients)
- 2) dry cough
- 3) **relative bradycardia** (also in Typhoid)
- 4) Confusion (may represent toxic encephalopathy).
- 5) **lymphopaenia**
- 6) **hyponatraemia** (SIADH),
- 7) renal failure, proteinuria
- 8) deranged liver function tests
- 9) pleural effusion: seen in around 30% of patients

Progresses to **bilateral** involvement in 50% of cases

Diagnosis:

- urinary antigen

Management:

1) Monotherapy:

- ⇒ **The newer quinolones** (especially **levofloxacin**) and **the newer macrolides** (especially **azithromycin**) are effective for treating legionellosis.
- ⇒ In comparison with erythromycin, they are more potent, have better tissue penetration and significantly less gastrointestinal toxicity.

2) Rifampin combined with erythromycin, combination therapy is now only recommended in patients who are failing standard therapy.

Psittacosis (parrot fever)

- a zoonotic disease caused by **Chlamydia psittaci**
- contracted from parrots cockatiels and budgerigars, and pigeons, sparrows, ducks, hens, gulls and many other species of bird.
- IP of 5–19 days,
- The symptoms of the disease range from inapparent illness to systemic illness with severe atypical pneumonia.
- High fevers, joint pains, diarrhea, **conjunctivitis**, **epistaxis**
- **Spleen enlargement** is common.

Complications:

- 1) endocarditis, myocarditis
- 2) hepatitis, , arthritis,
- 3) keratoconjunctivitis, and encephalitis may occasionally occur.

Diagnosis:

- Can be suspected if respiratory infection with **splenomegaly** and/or **epistaxis**.
- X-rays show patchy infiltrates or a **diffuse whiteout** of lung fields.
- **leukopenia**, **thrombocytopenia** and moderately elevated liver enzymes.
- **Culture** from respiratory secretions or increase in **antibody titers against C. psittaci**.
- **Typical inclusions** within macrophages in BAL.

Treatment:

- ☒ **Tetracyclines & chloramphenicol** are the drugs of choice at least 10–14 days after fever abates

Pneumocystis jiroveci pneumonia

- The term *Pneumocystis carinii* pneumonia (PCP) is still in common use
- *Pneumocystis jiroveci* is an **unicellular eukaryote**, generally classified as a fungus but some authorities consider it a protozoa
- PCP is the most common opportunistic infection in **AIDS**
- All patients with a **CD4 count < 200/mm** should receive PCP prophylaxis & pre CLL chemotherapy with **fludarabin** (as any of purine analogues).

Features:

- 1) Dyspnoea, **exercise induced desaturation**.
- 2) dry cough, fever
- 3) **Lymphopenia**
- 4) **Very few chest signs**
- 5) Pneumothorax **is a common complication of PCP**.

Extrapulmonary manifestations **are rare** (1-2% of cases), may cause

- 1) hepatosplenomegaly
- 2) lymphadenopathy
- 3) choroid lesions

Investigation:

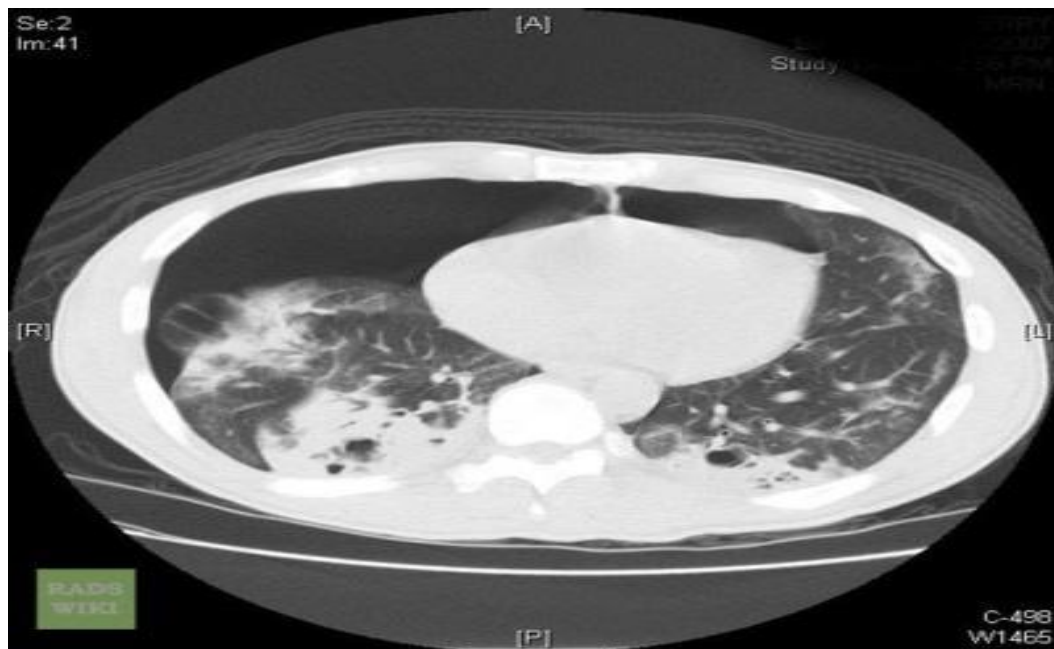
- 1) CXR: May be normal
 - ⇒ Typically shows bilateral interstitial pulmonary infiltrates but
 - ⇒ Can present with other x-ray findings e.g. lobar consolidation.
- 2) sputum often fails to show PCP,
- 3) Definitive diagnosis is by **bronchial alveolar lavage (BAL) with silver staining** (Silver stain shows **characteristic cysts**)

Management:

- 1) **co-trimoxazole**
- 2) If allergic to co-trimoxazole alternative therapy would be IV **pentamidine** or **clindamycin** with **primaquine**.
- 3) IV pentamidine in severe cases
- 4) **steroids if hypoxic** if **PO2 < 9.3** (70)
 - ⇒ steroids reduce risk of respiratory failure by 50% and death by a third
 - ⇒ It is important that steroids be started right away if indicated, because their purpose is to keep people stable during those first few days of treatment.
 - ⇒ long term steroid is immunosuppressive but 21 day tapering course has been shown to be safe and effective

- Patients often deteriorate after starting therapy for PCP as the pneumonitis worsens due to the inflammation associated with dying pneumocysts.
- Oral prednisolone is added to reduce the inflammatory effect.

-IV pentamidine----->Trypanosoma (sleeping sickness) or Suramine or Mersaloprol (late)



CT scan showing a large pneumothorax developing in a patient with *Pneumocystis jirovecii* pneumonia



Pneumocystis jirovecii pneumonia (PCP)

Diffuse diseases of the lung parenchyma 868
Granulomatous lung disease 868
Granulomatous lung disease with vasculitis 870
Idiopathic interstitial pneumonias (IIP) 872
Other types of diffuse lung disease 874
Pulmonary infiltration with eosinophilia 874
Extrinsic allergic alveolitis 876

Churg-Strauss syndrome

ANCA associated small-medium vessel vasculitis.

Features:

- 1) asthma
- 2) paranasal sinusitis
- 3) Blood eosinophilia (e.g. > 10%)
- 4) mononeuritis multiplex
- 5) pANCA positive in 60%

Leukotriene receptor antagonists may precipitate the disease

Goodpasture's syndrome

- Goodpasture's syndrome is rare condition
- Associated with:
 - ⇒ Pulmonary haemorrhage and
 - ⇒ Rapidly progressive glomerulonephritis.
- It is caused by **anti-glomerular basement membrane** (anti-GBM) antibodies against type **IV collagen**.
- Goodpasture's syndrome is more common in **men** (sex ratio 2:1)
- It has a **bimodal age** distribution (peaks in 20-30 and 60-70 age bracket).
- It is associated with **HLA DR2**.

Features:

- 1) pulmonary haemorrhage
- 2) followed by **RPGN** rapidly progressive glomerulonephritis

Factors which increase likelihood of pulmonary haemorrhage:

- 1) young males
- 2) smoking
- 3) inhalation of hydrocarbons
- 4) lower respiratory tract infection
- 5) pulmonary oedema

Investigations:

- 1) renal biopsy: **linear IgG deposits** along BM
- 2) **raised transfer factor** secondary to pulmonary haemorrhages

Management:

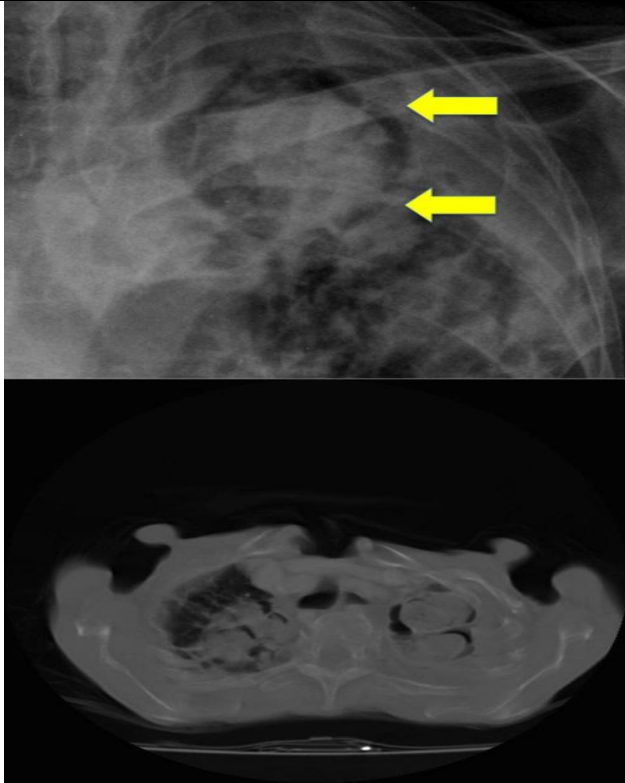
- 1) plasma exchange
- 2) steroids
- 3) cyclophosphamide

Aspergilloma

- An aspergilloma is a mycetoma (mass-like fungus ball) which often colonizes an existing lung cavity (e.g. secondary to tuberculosis, lung cancer or cystic fibrosis)
- Usually asymptomatic but features may include:
 - 1) Cough
 - 2) Haemoptysis (may be severe)

Investigations:

- 1) Chest x-ray: a solid opacity within a cavity often associated with a rim of air.
- 2) High titers IgG *Aspergillus* precipitins (95%)

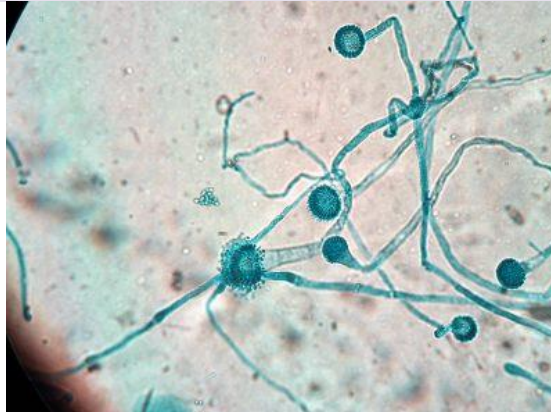


Aspergilloma in a patient with cavities secondary to previous tuberculosis infection. The close-up CXR and CT scan from the same patient demonstrate a rounded soft tissue attenuating masses located in a surrounding cavity.

Aspergillosis

- A fungal infection, and develops mainly in immunocompromised
- It is a leading cause of death in acute leukaemia and haemopoietic stem cell transplantation.
- Signs and symptoms include cough, haemoptysis, chest wall pain, fever and shock.
- It is often seen on chest x rays and CT scan, and demonstrates an air crescent sign.
- Other investigations include microscopy and the galactomannan test.

TTT: Intravenous amphotericin B



The slide shows the typical morphology of *Aspergillus fumigatus*.

Allergic bronchopulmonary aspergillosis

- Results from an allergy to **Aspergillus** spores.
- In the exam questions often give a history of **bronchiectasis** and **eosinophilia**.

Features:

- 1) **bronchoconstriction**: wheeze, cough, dyspnoea
- 2) **bronchiectasis** (proximal)
- 3) ABPA is characterized pathologically by mucoid impaction of the bronchi
- 4) sputum usually has brownish or greenish flecks which often contain aspergillus hyphae

Investigations:

- 1) eosinophilia
- 2) raised **IgE**
- 3) positive **radioallergosorbent** (RAST) test to Aspergillus
- 4) positive **IgG Aspergillus precipitins** (not as positive as in aspergilloma)
- 5) flitting CXR changes
- 6) CT: **Bronchocoeles** are a common feature of allergic bronchopulmonary aspergillosis (ABPA)

Management:

- 1) **steroids**
- 2) **itraconazole** is sometimes introduced as a second line agent



Chest x-ray of a 40-year-old woman with ABPA demonstrating a mass overlying the left hilum. In the right upper parahilar region a few ring shadow / tram track opacities are also noted, suggestive of bronchiectasis



CT scan from the same patient. CT reveals a branching lesion in the superior segment of the left lower lobe with classic finger in glove appearance which represents of mucous filling dilated bronchi (i.e. bronchocoeles).

A 28-year-old woman reports to your practice with a productive cough which gets worse at night, wheezing and difficulty in breathing for the last two months.

The sputum has some **brownish mucous plugs**. She now reports having fatigue on normal exertion. In the last two weeks she has developed haemoptysis.

There is a strong family history of atopy. She used to have asthma which she has outgrown.

On examination she is slightly dyspnoeic at rest. She is afebrile with a temperature of 36.6°C.

Her respiratory rate is 32 breaths/minute. On further examination the only significant finding is an expiratory wheeze.

The respiratory function tests were as follows:

Forced Expiratory Volume	1.40 L
Forced Vital Capacity	2.90 L
Peak Expiratory Flow Rate	200 L/min

The chest radiograph shows dilated bronchioles with a shadow in the mid-lung zones.

What is the likely diagnosis?

- a) Allergic bronchopulmonary aspergillosis
- b) Asthma
- c) Bronchiectasis
- d) Sarcoidosis
- e) Tuberculosis

The clinical picture above is one of allergic bronchopulmonary aspergillosis. It is very similar to asthma with a productive cough which is worse at night and wheezing. The sputum usually has brownish or greenish flecks which often contain aspergillus hyphae. The lung function tests show an obstructive pattern. The diagnosis should be confirmed by using any one of these tests; serum IgE levels of aspergillus, skin prick test for aspergillus or a radioallergosorbent test.

Asthma is the wrong answer. There are similarities with allergic bronchopulmonary aspergillosis clinically, however the differences are the presence of isolated aspergillus hyphae, recurrent episodes of bronchial obstruction, fever, malaise, expectoration of brownish mucus plugs, peripheral blood eosinophilia, and at times hemoptysis. Wheezing is not always evident, and some patients present with

asymptomatic pulmonary consolidation. ABPA is characterized pathologically by mucoid impaction of the bronchi, eosinophilic pneumonia, and bronchocentric granulomatosis in addition to the histologic features of asthma.

Bronchiectasis is the wrong answer. It is also very similar to allergic bronchopulmonary aspergillosis. The diagnosis is mainly clinical - daily mucopurulent sputum production lasting months to years. It also causes dyspnoea, chest pain, wheezing, fever, weakness, weight loss, recurrent chest infections and clubbing.

With sarcoidosis the patient can present with systemic complaints of fever, anorexia and arthralgia. There is also usually some dyspnoea on exertion, cough and chest pain with haemoptysis in 50% of the cases. The diagnosis is confirmed by a transbronchial biopsy.

With tuberculosis the patient would present with productive cough for more than two weeks, dyspnoea, chest pain, drenching night sweats and evening fevers.

Answer A

Extrinsic allergic alveolitis (EAA)

Hypersensitivity pneumonitis

- A condition caused by hypersensitivity induced lung damage due to a variety of inhaled organic particles.
- It is thought to be largely caused by **immune-complex mediated tissue damage (type III hypersensitivity)** although **delayed hypersensitivity (type IV)** is also thought to play a role in EAA, especially in the chronic phase.

Examples:

- 1) **Bird fanciers lung:** avian proteins. (It occurs most commonly among pigeon fanciers (اصحاب الببغاء and budgerigar owners مربو الحمام)
- 2) **Farmers lung:** spores of *Saccharopolyspora rectivirgula* (formerly *Micropolyspora faeni*)
- 3) **Mushroom workers lung:** thermophilic actinomycetes*
- 4) **Malt workers lung:** *Aspergillus clavatus*

*here the terminology is slightly confusing as thermophilic actinomycetes is an umbrella term covering strains such as *Micropolyspora faeni*



Malt workers (عامل الشعير)

Presentation:

- 1) acute: SOB, dry cough, fever
Symptoms may develop 4- 6 hrs after exposure to allergen and last 12 hours up to several days following removal of the antigen.
- 2) Chronic

Patients present with a progressive dyspnoea on exertion. Inspiratory crackles are heard on auscultation of the lungs. CXR shows fine linear opacities in the upper lobes which may progress to honeycombing.

The diagnosis of HP is based on typical clinical, radiological and lung function changes in the presence of an identified source of antigen with positive precipitating antibodies in the patient's serum to the causal antigen.

Improvement of clinical abnormalities following avoidance of the causal antigen helps confirm the diagnosis.

Investigation:

- 1) chest x-ray: upper/mid-zone fibrosis
- 2) bronchoalveolar lavage BAL: **lymphocytosis**
- 3) blood: **NO eosinophilia**

Pulmonary eosinophilia

Causes of pulmonary eosinophilia

- 1) Churg-Strauss syndrome
- 2) Allergic bronchopulmonary aspergillosis (ABPA)
- 3) Löffler's syndrome
- 4) Eosinophilic pneumonia
- 5) Hypereosinophilic syndrome
- 6) Tropical pulmonary eosinophilia
- 7) Nitrofurantoin, sulphonamides
- 8) Less common: Wegener's granulomatosis

Löffler's syndrome

- thought to be due to parasites such as *Ascaris lumbricoides* causing an alveolar reaction
- Presents with a fever, cough and night sweats which often last for less than 2 weeks.
- generally a self-limiting disease
- transient CXR shadowing and blood eosinophilia

Tropical pulmonary eosinophilia

- associated with *Wuchereria bancrofti* infection

Lung fibrosis

- It is important in the exam to be able to differentiate between conditions causing predominately upper or lower zone fibrosis.
- It should be noted that the more common causes (cryptogenic fibrosing alveolitis, drugs) tend to affect the lower zones

Fibrosis predominately affecting the upper zones:

- 1) extrinsic allergic alveolitis
- 2) coal worker's pneumoconiosis (progressive massive fibrosis)
- 3) silicosis
- 4) sarcoidosis, tuberculosis
- 5) histiocytosis
- 6) ankylosing spondylitis (rare)

Fibrosis predominately affecting the lower zones:

- 1) cryptogenic fibrosing Alveolitis (IPF)
- 2) most connective tissue disorders (except ankylosing spondylitis)
- 3) drug-induced: amiodarone, bleomycin, methotrexate
- 4) asbestosis

كل فوق osis

تحت asbestosis عدا

Silicosis usually results in small nodular opacities in the mid and upper zones. There may be associated hilar gland enlargement which may calcify producing characteristic 'eggshell' calcification. These radiological shadows are not usually associated with symptoms or loss of lung function.



CT scan showing advanced pulmonary fibrosis including 'honeycombing'

Drugs causing lung fibrosis

- 1) Amiodarone
- 2) Busulphan, bleomycin (cytotoxic agents)
- 3) Methotrexate, sulfasalazine, gold (anti-rheumatoid drugs)
- 4) Nitrofurantoin
- 5) Ergot-derived dopamine receptor agonists (bromocriptine, cabergoline, pergolide)

Idiopathic pulmonary fibrosis (IPF)

- previously termed cryptogenic fibrosing alveolitis
- A chronic lung condition characterised by progressive fibrosis of the interstitium of the lungs.
- Whilst there are many causes of lung fibrosis (e.g. medications, connective tissue disease, asbestos) the term IPF is reserved when no underlying cause exists.
- IPF is typically seen in patients aged 50-70 years and is twice as common in men.

Features:

- 1) Progressive exertional dyspnoea
- 2) Dry cough
- 3) Bibasal crackles on auscultation
- 4) **Clubbing**

Diagnosis:

- 1) **Spirometry:**
 - ⇒ Classically a restrictive picture (FEV1 normal/decreased, FVC decreased, FEV1/FVC increased)
- 2) **Impaired gas exchange:** reduced transfer factor (TLCO)
- 3) **Imaging:**
 - ⇒ CXR
 - ⇒ bilateral interstitial shadowing (Typically small, irregular, peripheral opacities 'ground-glass' Later progressing to 'honeycombing')
 - ⇒ **high-resolution CT scanning HRCT** is **the investigation of choice** and required to make a diagnosis of IPF
- 4) **ANA positive in 30%, rheumatoid factor positive in 10%** but this does not necessarily mean that the fibrosis is secondary to a connective tissue disease. Titers are usually low

Management:

- 1) Pulmonary rehabilitation
- 2) Very few medications have been shown to give any benefit in IPF.
 - ⇒ There is some evidence that **pirfenidone** (an antifibrotic agent) may be useful in selected patients
- 3) Many patients will require supplementary oxygen and eventually a lung transplant

Prognosis:

- poor, average life expectancy is around 3-4 years



Chest X-ray shows sub-pleural reticular opacities that increase from the apex to the bases of the lungs



CT scan showing advanced pulmonary fibrosis including 'honeycombing'

Sarcoidosis

- Multisystem disorder of unknown aetiology characterised by **non-caseating granulomas**.
- It is more common in young adults and in people of **African** descent.
- Sarcoidosis remits without treatment in approximately two-thirds of people

Features:

1) Acute: **Lofgren's syndrome:**

- ⇒ erythema nodosum,
 - ⇒ bilateral hilar lymphadenopathy,
 - ⇒ swinging fever,
 - ⇒ polyarthralgia (sarcoidosis typically targets the **ankle joint**.)
- 2) insidious: dyspnoea, non-productive cough, malaise, weight loss
- 3) **lupus pernio** erythematous nodular lesions on the cheek, nose, forehead and chin.
- 4) hypercalcaemia: macrophages inside granulomas cause an increased conversion of vitamin D to its active form (1,25-dihydroxycholecalciferol), may lead to nephropathy
- 5) **cranial nerve palsies**,
- 6) **Lymphadenopathy and**
- 7) **hepatosplenomegaly**

Investigation:

- 1) **Diagnostic : tissue biopsy: non-caseating granulomas**
- 2) ACE levels:
- ⇒ It has a sensitivity 60% and
 - ⇒ specificity 70% and is therefore not reliable in the diagnosis of sarcoidosis although
 - ⇒ They may have a role in **monitoring disease activity**.
- 3) Routine bloods may show hypercalcaemia (seen in 10% of patients) and a **raised ESR**
- 4) **A chest x-ray** may show the following changes:
- ✓ stage 0 = normal
 - ✓ stage 1 = bilateral hilar lymphadenopathy (BHL)
 - ✓ stage 2 = BHL + interstitial infiltrates
 - ✓ stage 3 = diffuse interstitial infiltrates only
 - ✓ stage 4 = diffuse fibrosis

Other investigations*

- 1) spirometry: may show a restrictive defect
- 2) gallium-67 scan: not used routinely

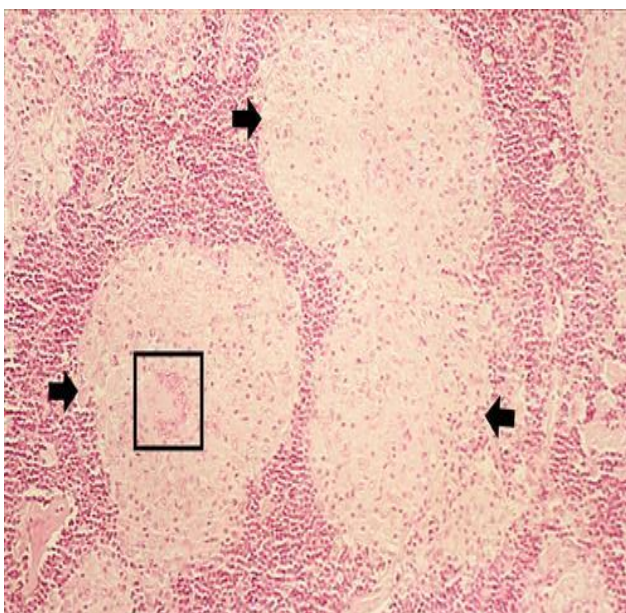
*the Kveim test (where part of the spleen from a patient with known sarcoidosis is injected under the skin) is no longer performed due to concerns about cross-infection



Chest x-ray and CT scan showing stage 2 sarcoidosis with both bilateral hilar lymphadenopathy + interstitial infiltrates. The reticulonodular opacities are particularly noted in the upper zones.

The CT of the chest demonstrates diffuse areas of nodularity predominantly in a peribronchial distribution with patchy areas of consolidation particularly in the upper lobes. There is some surrounding ground glass opacities. No gross reticular changes to suggest fibrosis.

The lymph node biopsy specimen shown contains three large granulomata (arrowed, below). In addition, the granuloma at the bottom left of the picture also contains a multinucleate Langhans giant cell (in box). There is no evidence of caseation.



The chest x ray shows bilateral reticulonodular shadowing and bilateral hilar lymphadenopathy.

There is lymphopenia, hyperglobulinaemia and hypercalcaemia.

Sarcoidosis management:

- Sarcoidosis remits without treatment in approximately two-thirds of people

Indications for steroids

- 1) Patients with chest x-ray stage 2 or 3 disease who have moderate to severe or progressive symptoms.
 - ☒ Patients with asymptomatic and stable stage 2 or 3 disease who have only mildly abnormal lung function **do not require treatment**
- 2) Hypercalcaemia
- 3) Eye, heart or neuro involvement

Sarcoidosis prognostic features:

Factors associated with poor prognosis:

- 1) black people
- 2) insidious onset, symptoms > 6 months
- 3) CXR: stage III-IV features
- 4) extrapulmonary manifestations: e.g. lupus pernio, splenomegaly
- 5) absence of erythema nodosum

Syndromes associated with sarcoidosis:

Lofgren's syndrome:

- An acute form sarcoidosis characterised by:
 - 1) bilateral hilar lymphadenopathy (BHL),
 - 2) erythema nodosum,
 - 3) Fever and polyarthralgia.
- It typically occurs in young females and carries an excellent prognosis.

Heerfordt's syndrome (uveo-parotid fever)

- Fever and
- **Uveitis** secondary to sarcoidosis
- **Parotid** enlargement,

Mikulicz syndrome:

- There is enlargement of the **parotid** and **lacrimal glands** due to sarcoidosis, tuberculosis or lymphoma
- This term is now considered outdated and unhelpful by many as there is a confusing overlap with Sjogren's syndrome

Bilateral hilar lymphadenopathy

The most common causes of bilateral hilar lymphadenopathy are:

- 1) sarcoidosis and
- 2) tuberculosis

Other causes include:

- 1) lymphoma/other malignancy
- 2) pneumoconiosis e.g. berylliosis (non-caseating granuloma occupational disease)
- 3) fungi e.g. histoplasmosis, coccidioidomycosis

Lung cancer

Types:

- 1) Squamous:----- 35%
- 2) Adenocarcinoma:-- 30%
- 3) Small (oat) cell:----- 15%
- 4) Large cell:-----10%
- 5) Other c. 5%

Other tumours:

1) Bronchoalveolar cell carcinoma:

- ☒ not related to smoking,
- ☒ ++sputum,
- ☒ Classically presents with progressive breathlessness and the production of large amounts of sputum (**bronchorrhoea**)
- ☒ Almost a half of patients are diagnosed on routine CXR, usually demonstrating a **peripheral lesion**.
- ☒ Its name arises from its pattern of growth along the alveolar walls without actually destroying them.
- ☒ It is an **adenocarcinoma**.
- ☒ In those whose tumour is not resectable, prognosis is poor.

2) Bronchial adenoma:

- ☒ mostly carcinoid

Lung cancer risk factors:

- 1) **Smoking:** increases risk of lung ca by a **factor of 10**
- 2) Asbestos - increases risk of lung ca by a **factor of 5**
- 3) Arsenic
- 4) Radon
- 5) Nickel
- 6) Chromate
- 7) Aromatic hydrocarbon
- 8) Cryptogenic fibrosing alveolitis (IPF)

Factors that are NOT related:

- coal dust

Smoking and asbestos are synergistic, i.e. a smoker with asbestos exposure has a $10 * 5$ = **50 times** increased risk

Central lesions: small cell, squamous cell, Bronchial adenoma

Peripheral lesion: bronchoalveolar cell carcinoma, adenocarcinoma

Non-small cell Lung cancer

There are three main subtypes of non-small cell lung cancer:

A) Squamous cell cancer (35%)

- Typically **central** (cavitating lung lesion)
- Associated with **parathyroid hormone-related protein** (PTHrP) secretion → hypercalcaemia
- **Hyperthyroidism** due to ectopic TSH
- Strongly associated with finger **clubbing**
- **Hypertrophic pulmonary osteoarthropathy** (HPOA)

B) Adenocarcinoma (30%)

- **most common type of lung cancer in non-smokers**, although the majority of patients who develop lung adenocarcinoma are smokers
- typically **located on the lung periphery**
- **gynecomastia**

C) Large cell lung carcinoma (10%)

Management of Non-small cell Lung cancer

- 1) Only 20% suitable for surgery
- 2) **Mediastinoscopy** performed prior to surgery as CT does not always show mediastinal lymph node involvement
- 3) Curative or palliative **radiotherapy**
- 4) Poor response to chemotherapy

Surgery contraindications:

- 1) assess general health
- 2) stage IIIb or IV (i.e. metastases present)
- 3) FEV1 < 1.5 litres is considered a general cut-off point*
- 4) malignant pleural effusion
- 5) tumour near hilum
- 6) vocal cord paralysis
- 7) SVC obstruction

* However if FEV1 < 1.5 for lobectomy or < 2.0 for pneumonectomy then some authorities advocate further lung function tests as operations may still go ahead based on the results

Small Cell Lung Cancer (15%)

Features:

- 1) Usually **central**
- 2) Arise from **APUD cells** (Amine Precursor Uptake Decarboxylase)
- 3) Associated with ectopic **ADH**, **ACTH** secretion
 - ⇒ ADH → hyponatraemia
 - ⇒ ACTH → Cushing's syndrome
 - ⇒ ACTH secretion can cause:
 - ✓ bilateral adrenal hyperplasia,
 - ✓ the high levels of cortisol can lead to hypokalaemic alkalosis
- 4) **Lambert-Eaton syndrome**: antibodies to voltage gated calcium channels causing myasthenic like syndrome

*an acronym for

- Amine - high amine content
- Precursor Uptake - high uptake of amine precursors
- Decarboxylase - high content of the enzyme decarboxylase

Management:

- 1) Usually metastatic disease by time of diagnosis
- 2) Patients with very early stage disease (**T1-2a, N0, M0**) are now considered for **surgery**. NICE support this approach in their 2011 guidelines
- 3) however, most patients with limited disease receive a **combination** of **chemotherapy** and **radiotherapy**
- 4) Patients with more extensive disease are offered **palliative chemotherapy**



CT scan showing small cell lung cancer with multiple pulmonary nodules and extensive mediastinal nodal metastases.

Paraneoplastic features of lung cancer

- squamous cell: PTHrp, TSH, clubbing, HPOA
 - small cell: ADH, ACTH, Lambert-Eaton syndrome
-
- The brain is a frequent site of first relapse in patients after complete therapeutic response.
 - Prophylactic cranial irradiation should therefore be considered for patients with Small CLC who have a response to initial chemotherapy.
 - Prophylactic cranial irradiation based on randomised clinical trials largely applied to patients with limited-stage SCLC has demonstrated a decrease in the risk of intracranial relapse from 40% to 20% and improved long term survival by approximately 5%.

Lung carcinoid (1%) **(Bronchial adenomas)**

- The vast majority of **bronchial adenomas** are carcinoid tumours, arise from the amine precursor uptake and decarboxylation (APUD) system, like small cell tumours
- Lung carcinoid accounts 1% of lung tumours and for 10% of carcinoid tumours.
- The term bronchial adenoma is being phased out.

Features:

- 1) typical age = 40-50 years
- 2) smoking not risk factor
- 3) slow growing: e.g. long history of cough, recurrent haemoptysis
- 4) often **centrally** located and not seen on CXR
- 5) '**cherry red ball**' often seen on bronchoscopy
- 6) carcinoid syndrome itself is **rare**

Management:

- 1) Surgical resection
- 2) If no metastases then 90% survival at 5 years

Paraneoplastic features in Lung cancer

A) Squamous cell:

- 1) parathyroid hormone-related protein (PTH-rp) secretion causing hypercalcaemia
- 2) hyperthyroidism due to ectopic TSH
- 3) hypertrophic pulmonary osteoarthropathy (HPOA)
- 4) clubbing

B) Adenocarcinoma:

- Gynaecomastia

C) Small cell:

- 1) ADH
- 2) ACTH (Increased cortisol)- not typical, hypertension, hyperglycaemia, hypokalaemia, alkalosis and muscle weakness are more common than buffalo hump etc
- 3) Lambert-Eaton syndrome



Hypertrophic pulmonary osteoarthropathy is a proliferative periostitis involving that typically involves the long bones. It is often painful.

Laryngeal cancer

- Initial therapy for stages I and II is **radiation therapy** or **surgery**.
- External beam radiation is the curative and function sparing treatment for this patient who has stage I and II laryngeal cancer.
- In the setting of lymph node-positive or locally advanced disease, the benefit of concurrent **chemoradiotherapy** is recommended.
- **Cetuximab** is a monoclonal antibody and is effective when combined with radiation, it has been found to improve local control and overall survival rates.



Cavitating lung carcinoma

This is a thick walled irregular cyst with an associated enlarged right hilum responsible for the soft tissue adjacent to the right pulmonary artery.

The TNM Classification of Malignant Tumours (TNM)

A cancer staging system that describes the extent of cancer in a patient's body

- T describes the size of the tumor and whether it has invaded nearby tissue,
- N describes regional lymph nodes that are involved.
- M describes distant metastasis (spread of cancer from one body part to another),

Primary Tumor (T)

TX	• Primary tumor cannot be assessed, or • tumor proven by the presence of malignant cells in sputum or bronchial washings but not visualized by imaging or bronchoscopy
T0	No evidence of primary tumor
Tis	Carcinoma in situ
T1	• Tumor 3 cm or less in greatest dimension, • surrounded by lung or visceral pleura, without bronchoscopic evidence of invasion more proximal than the lobar bronchus (for example, not in the main bronchus)
T1a	Tumor 2 cm or less in greatest dimension
T1b	Tumor more than 2 cm but 3 cm or less in greatest dimension
T2	Tumor more than 3 cm but 7 cm or less or tumor with any of the following features (T2 tumors with these features are classified T2a if 5 cm or less): • involves main bronchus, 2 cm or more distal to the carina; • invades visceral pleura (PL1 or PL2); • associated with atelectasis or obstructive pneumonitis that extends to the hilar region but does not involve the entire lung
T2a	Tumor more than 3 cm but 5 cm or less in greatest dimension
T2b	Tumor more than 5 cm but 7 cm or less in greatest dimension
T3	Tumor more than 7 cm or one that directly invades any of the following : • parietal pleural (PL3), • chest wall (including superior sulcus tumors), • diaphragm, phrenic nerve, • mediastinal pleura, parietal pericardium; or Tumor in the main bronchus less than 2 cm distal to the carina ¹ but without involvement of the carina; or associated atelectasis or obstructive pneumonitis of the entire lung or separate tumor nodule(s) in the same lobe

T4	Tumor of any size that invades any of the following: • mediastinum, heart, great vessels, • trachea, recurrent laryngeal nerve, esophagus, • vertebral body, carina, • separate tumor nodule(s) in a different ipsilateral lobe
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Distant Metastasis (M)

M0	No distant metastasis
M1	Distant metastasis
M1a	• Separate tumor nodule(s) in a contralateral lobe, • tumor with pleural nodules or malignant pleural (or pericardial) effusion
M1b	Distant metastasis (in extrathoracic organs)

Regional Lymph Nodes (N)

NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastases
N1	Metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes and intrapulmonary nodes, including involvement by direct extension
N2	Metastasis in ipsilateral mediastinal and/or subcarinal lymph node(s)
N3	• Metastasis in contralateral mediastinal, contralateral hilar, • ipsilateral or contralateral scalene, or • supraclavicular lymph node(s)

Occupational lung disease

Asbestos and the lung

Asbestos can cause a variety of lung disease from benign pleural plaques to mesothelioma.

A) Pleural plaques:

- Pleural plaques are **benign** and **do not undergo malignant change**.
- They are **the most common form of asbestos related lung disease**
- generally occur after a latent period of 20-40 years

B) Pleural thickening:

- Asbestos exposure may cause diffuse pleural thickening (**bilateral**) in a similar pattern to that following TB or Bacterial empyema or haemothorax (causes of unilateral pleural thickening).
- The underlying pathophysiology is not fully understood.

C) Asbestosis:

- diffuse interstitial fibrosis secondary to asbestos inhalation
- Asbestosis typically causes **lower lobe fibrosis**.
- The severity of asbestosis is **related to the length of exposure**.
- The **latent period is typically 15-30 years**.
- As with other forms of lung fibrosis the most common symptoms are shortness-of-breath and reduced exercise tolerance.

D) Mesothelioma:

- Mesothelioma is a malignant disease of the pleura.
- Crocidolite (blue) asbestos is the most dangerous form. **الاسبستوس الازرق**
- Very limited exposure can cause disease.

Possible features:

- 1) progressive shortness-of-breath
- 2) chest pain
- 3) pleural effusion

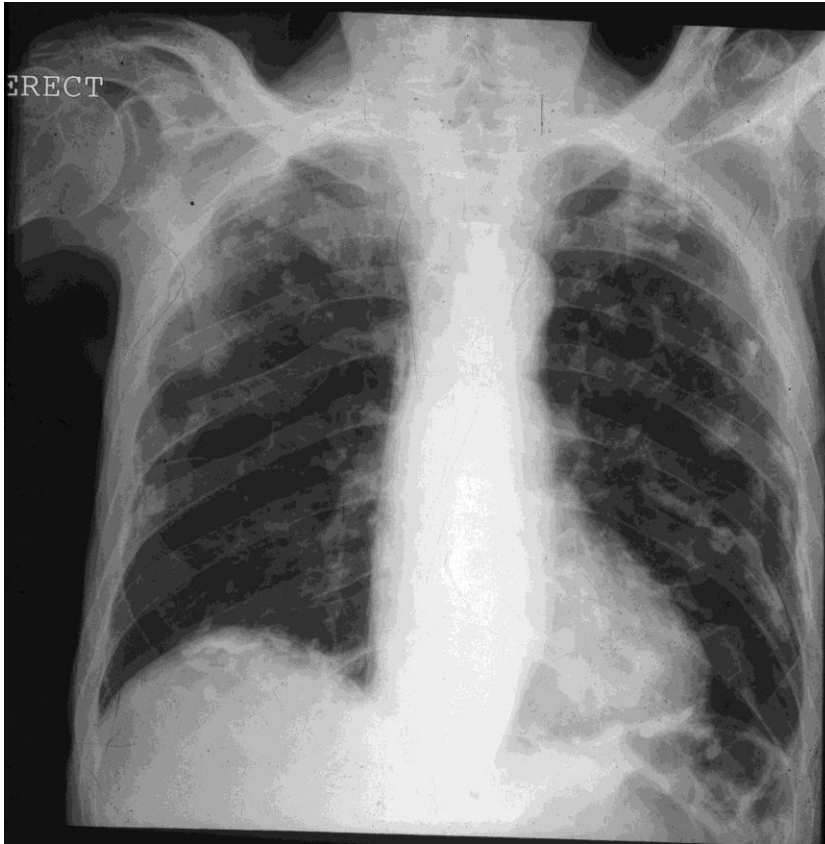
Management:

- 1) Patients are usually offered **palliative chemotherapy**
- 2) There is also a **limited role for surgery and radiotherapy**.
- 3) Unfortunately the **prognosis is very poor**
- 4) Median survival from diagnosis of **8-14 months**

E) Lung cancer

- Asbestos exposure increases risk of lung ca by a **factor of 5**
- Also has a synergistic effect with cigarette smoke.

Smoking and asbestos are synergistic, i.e. a smoker with asbestos exposure has a $10 * 5 = 50$ **times** increased risk



The x ray shows extensive pleural plaques and the clinical history would suggest previous exposure to asbestos.

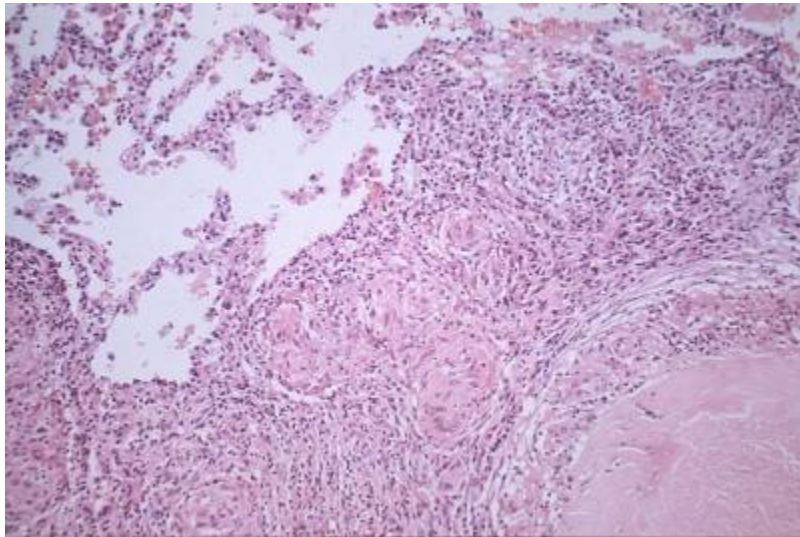
Silicosis

- Silicosis is a fibrotic lung disease associated with the inhalation of silicon dioxide (silica).
- It is usually found in quarry workers (عمال المحاجر) or miners (عمال المناجم) and also sandblasters, pottery workers (عمال الفخار) and stonemasons (عمال البناء) (if the dust contains quartz).
- Diagnosis is made on industrial history and typical chest x ray changes.
- The pathognomonic radiological changes are **hilar eggshell calcification**.
- Silicosis is a risk factor for developing **TB** (silica is toxic to macrophages)

Features:

- 1) **Fibrosing** lung disease (upper lung zone)
- 2) **Egg-shell calcification** of the hilar lymph nodes

Disease	Agent	Effects
Aluminosis	Alum, and al. oxide	Fibrosis, bullae, pneumothorax
Asbestosis	Asbestos	Pleural plaques, lung cancer, mesothelioma
Byssinosis	Cotton, flax, hemp	Airway obstruction, loss of elasticity
Metal fume fever	Cadmium, cobalt, nickel, zinc and others	Chemical pneumonitis
Occupational asthma	Western Red Cedar and others	Reversible airway obstruction
Siderosis	Iron oxide	Dust deposits
Silicosis	Silica	Dust deposits and fibrosis
Talcosis	Talc, hydrated Mg. silicates	Perivascular fibrosis



The lung histology shows non-caseating granulomata, a characteristic feature of berylliosis.

Disorders of the chest wall and pleura

Mesothelioma

- Malignancy of mesothelial cells of pleura
- Metastases to contralateral lung and peritoneum
- Right lung affected more often than left

Features:

- 1) Dyspnoea, weight loss, chest wall pain
- 2) Clubbing
- 3) 30% present as painless pleural effusion
- 4) Only 20% have pre-existing asbestosis
- 5) Very limited exposure can cause disease.
- 6) History of asbestos exposure in 85-90%, {Crocidolite (blue)}
- 7) Latent period of 30 years

Diagnosis:

- 1) Suspicion is normally raised by a chest x-ray showing either a pleural effusion or pleural thickening
- 2) The next step is normally a pleural CT
- 3) If a pleural effusion is present fluid should be sent for MC&S, biochemistry and cytology (but cytology is only helpful in 20-30% of cases)
- 4) **Local anaesthetic thoracoscopy biopsy** (Video-assisted thoracoscopic surgery VATS biopsy) **منظار بلوری** is increasingly used to investigate cytology negative exudative effusions as it has a high **diagnostic** yield (**around 95%**)
- 5) If an area of pleural nodularity is seen on CT then an image-guided pleural biopsy may be used

Management:

- 1) Symptomatic
- 2) Industrial compensation
- 3) Chemotherapy, Surgery if operable
- 4) Prognosis poor, median survival 12 months



The diagnosis is a mesothelioma. There is a large rind of soft tissue related to the left chest wall.

This is a malignant process as there is destruction of the associated rib excluding the other diagnoses.

Pleural effusion

Exudate (> 35 g/L protein)	Transudate (< 25 g/L protein)
A) infection: pneumonia, TB, subphrenic abscess B) connective tissue disease: RA, SLE C) neoplasia: lung cancer, mesothelioma, metastases D) pancreatitis E) pulmonary embolism F) Dressler's syndrome G) yellow nail syndrome	A) heart failure B) hypoalbuminaemia (liver disease, nephrotic syndrome, malabsorption) C) hypothyroidism D) Meigs' syndrome

Pleural effusion investigation

The British Thoracic Society (BTS) produced guidelines in 2010 covering the investigation of patients with a pleural effusion:

A) **Imaging:**

- 1) posterioranterior (PA) chest x-rays should be performed in all patients
- 2) ultrasound is recommended: it increases the likelihood of successful pleural aspiration and is sensitive for detecting pleural fluid septations

B) **Pleural aspiration:**

- as above, ultrasound is recommended to reduce the complication rate
- a 21G needle and 50ml syringe should be used
- fluid should be sent for pH, protein, lactate dehydrogenase (LDH), cytology and microbiology
 - ⇒ exudates have a protein level > 35 g/L,
 - ⇒ transudates have a protein level < 25 g/L

Light's criteria were developed in 1972 to help distinguish between a transudate and exudates. The BTS recommend using the criteria for borderline cases:

- If the protein level is between 25-35 g/L, Light's criteria should be applied.
- **An exudate is likely if at least one of the following criteria are met:**
 - 1) pleural fluid protein divided by serum protein >0.5
 - 2) pleural fluid LDH divided by serum LDH >0.6
 - 3) pleural fluid LDH more than two-thirds the upper limits of normal serum LDH

Pleural infection:

- 1) all patients with a pleural effusion in association with sepsis or a pneumonic illness require diagnostic pleural fluid sampling
- 2) if the fluid is purulent or turbid/cloudy a **chest tube should be placed to allow drainage**
- 3) if the fluid is clear but the **pH is less than 7.2** in patients with suspected pleural infection a **chest tube** should be placed

Other characteristic pleural fluid findings:

- 1) **low glucose:** rheumatoid arthritis, tuberculosis
- 2) **raised amylase:** pancreatitis, oesophageal perforation
- 3) **heavy blood staining:** mesothelioma, pulmonary embolism, tuberculosis

The pleural glucose level less than 3.3 mmol/L are found in

- Malignancy
- Rheumatoid arthritis
- Tuberculosis.
- Empyema
- Lupus
- Oesophageal rupture and

Pneumothorax

- The British Thoracic Society (BTS) published updated guidelines for the management of spontaneous pneumothorax in 2010.
- A pneumothorax is termed primary if there is no underlying lung disease and secondary if there is.

Primary Pneumothorax:

Recommendations include:

- 1) If the rim of air is **< 2cm** and the patient is **not short of breath** then **discharge** should be considered & **CXR after 2 weeks**.
- 2) **otherwise aspiration** should be attempted
- 3) **if this fails** (defined as **> 2 cm** or still short of breath) then a **chest drain** should be inserted
- 4) patients should be advised to **avoid smoking** to reduce the risk of further episodes
- 5) the lifetime risk of developing a pneumothorax
 - ⇒ in healthy smoking men is around 10%
 - ⇒ non-smoking men → 0.1% in

Secondary Pneumothorax:

All patients should be admitted for at least 24 hours

- 1) **If the pneumothorax is less the 1cm** then the BTS guidelines suggest:
 - ⇒ **giving oxygen** (high flow O₂) and
 - ⇒ **admitting for 24 hours**
- 2) **If the patient is:**
 - ✓ **50 years old** and the **rim of air is > 2cm** and/or
 - ✓ **The patient is short of breath** then
 - ⇒ **A chest drain should be inserted.**

Otherwise **aspiration** should be attempted if the **rim of air is between 1-2cm**.

If aspiration fails (i.e. pneumothorax is still greater than 1cm) a **chest drain** should be inserted.

- For a second unilateral pneumothorax in a fit individual is referral for bullectomy and pleurectomy. This is conducted under video assisted guidance, video assisted thoracoscopic surgery (VATS), until then, diving and flying are contraindicated.
- Regarding scuba diving, the BTS guidelines state: 'Diving should be permanently avoided unless the patient has undergone bilateral surgical pleurectomy and has normal lung function and chest CT scan postoperatively.'
- Pleurodesis could be considered in elderly or frail individuals.

Iatrogenic Pneumothorax:

Recommendations include:

- 1) less likelihood of recurrence than spontaneous pneumothorax
- 2) majority will resolve with observation, if treatment is required then aspiration should be used
- 3) ventilated patients need chest drains, as may some patients with COPD

Tension pneumothorax:

There is a mediastinal shift away from the midline

Where there is a tension pneumothorax neither oxygen alone nor needle aspiration are the definitive treatment and a chest tube must be inserted.

Questions sometimes discuss the size of the pneumothorax in percentage terms rather than giving the interpleural distance. A variety of formulas have been proposed to convert between the two.

As a very general rule of thumb:

Average interpleural distance	Approximate size of pneumothorax
0.5 cm	10%
1 cm	15 %
2 cm	30%
3 cm	45%
4 cm	60%

A pneumothorax of 20% is therefore within the 2 cm limit suggested by the British Thoracic Society for observation, if the patient is not short of breath

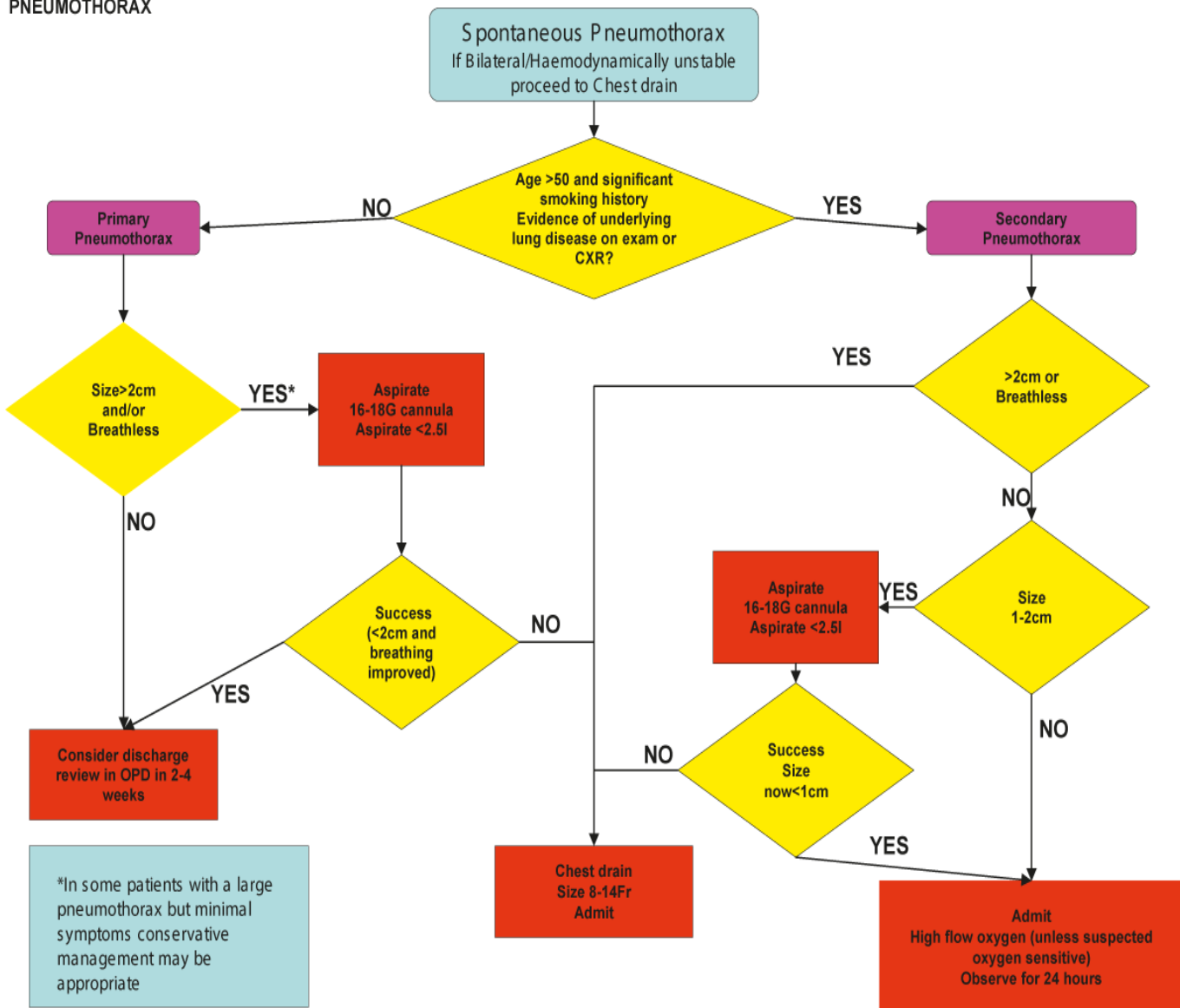
Small bore drains are just as effective as large bore drains and are less painful when in situ.

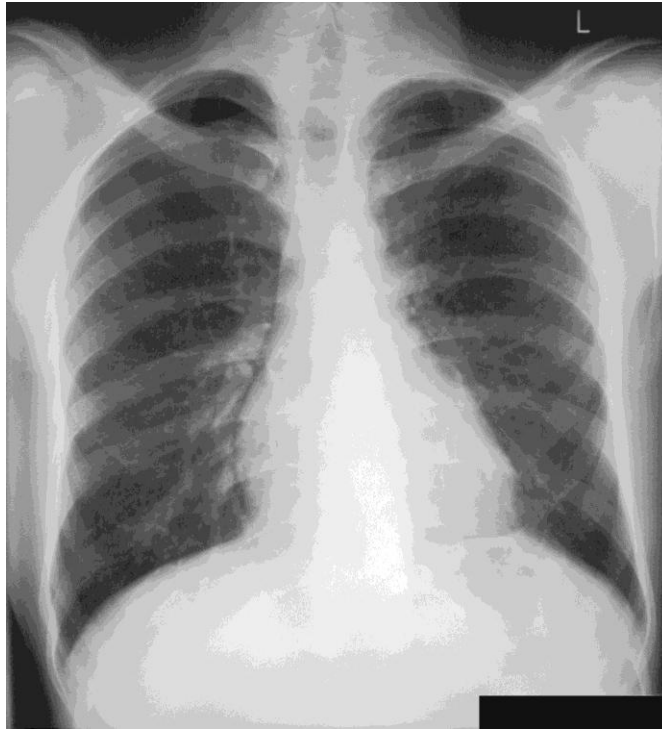
The most appropriate point for chest drain insertion is in the 'safe triangle' in the **mid-axillary** line. This reduces injury to the internal mammary artery, muscle, liver and spleen.

Scarring from insertion is less obvious than in the second intercostal space and mid-clavicular line, particularly in women.

Loculated apical pneumothoraces (as demonstrated by a CT scan) may be drained using a **posteriorly sited** (suprascapular) apical tube.

MANAGEMENT OF SPONTANEOUS PNEUMOTHORAX





The slide shows a small right apical pneumothorax less than 2 cm in size



The slide shows a large left-sided tension pneumothorax.

The left hemithorax is hyperinflated with loss of lung markings peripherally. This is particularly noticeable in the left lower zone. There is also a mediastinal shift away from the midline towards the right.

This is a classical presentation of pneumothorax: young fit male (often tall) who develops chest pain and shortness of breath while exercising.

Fitness to fly

The Civil Aviation Authority (CAA) has issued guidelines on air travel for people with medical conditions; please see the link provided.

Cardiovascular disease:

- unstable angina, uncontrolled hypertension, uncontrolled cardiac arrhythmia, decompensated heart failure, severe symptomatic valvular disease: should not fly
- uncomplicated MI: may fly after 7-10 days
- complicated MI: after 4-6 weeks
- CABG: after 10-14 days
- PCI: after 5 days

Respiratory disease:

- pneumonia: should be 'clinically improved with no residual infection'
- Pneumothorax: absolute contraindication, the CAA suggest patients may travel 2 weeks after successful drainage if there is no residual air.
- The British Thoracic Society used to recommend not travelling by air for a period of 1 week post check x-ray

Pregnancy:

- most airlines do not allow travel after 36 weeks for a single pregnancy and after 32 weeks for a multiple pregnancy
- most airlines require a certificate after 28 weeks confirming that the pregnancy is progressing normally

Surgery:

- travel should be avoided for 10 days following abdominal surgery
- laparoscopic surgery: after 24 hours
- colonoscopy: after 24 hours
- following the application of a plaster cast, the majority of airlines restrict flying for 24 hours on flights < 2 hours or 48 hours for longer flights

Haematological disorders:

- patients with a haemoglobin > 8 g/dl may travel without problems (assuming there is no coexisting condition such as cardiovascular or respiratory disease)

Pulmonary embolism

Investigation:

- We know from experience that few patients (around 10%) present with the medical student textbook triad of **pleuritic chest pain, dyspnoea and haemoptysis**.
- Pulmonary embolism can be difficult to diagnose as it can present with virtually any cardiorespiratory symptom/sign depending on its location and size.

So which features make pulmonary embolism more likely?

- The PIOPED study¹ in 2007 looked at the frequency of different symptoms and signs in patients who were diagnosed with pulmonary embolism.
- The relative frequency of common clinical signs is shown below:
 - 1) **Tachypnea (RR >16/min) - 96%**
 - 2) **Crackles - 58%**
 - 3) **Tachycardia (HR >100/min) - 44%**
 - 4) **Fever (>37.8C) - 43%**
- It is interesting to note that the Well's criteria for diagnosing a PE use tachycardia rather than tachypnoea.

2012 NICE guidelines

- All patients with symptoms or signs suggestive of a PE should have a history taken, examination performed and a **chest x-ray** to exclude other pathology.
- If a PE is still suspected a two-level PE **Wells score** should be performed:

Clinical feature	Points
Clinical S & S of DVT (minimum of leg swelling and pain with palpation of the deep veins)	3
An alternative diagnosis is less likely than PE (PE is #1 diagnosis)	3
Heart rate > 100 beats per minute	1.5
Immobilisation for more than 3 days or surgery in the previous 4 weeks	1.5
Previous DVT/PE	1.5
Haemoptysis	1
Malignancy (on treatment, treated in the last 6 months, or palliative)	1

Traditional interpretation:

- High score: >6.0
- Moderate score: 2.0 to 6.0
- Low score: <2.0

Alternate interpretation score:

- > 4 - PE likely. Consider diagnostic imaging
- ≤ 4 - PE unlikely. Consider D-dimer to rule out PE.

If a PE is 'likely' (> 4 points)

- ⇒ Arrange an immediate computed tomography pulmonary angiogram (CTPA).
- ⇒ If there is a delay in getting the CTPA then give LMWH until the scan is performed

If a PE is 'unlikely' (4 points or less)

- ⇒ Arrange a D-dimer test.
 - ⇒ If this is positive arrange an immediate (CTPA).
 - ⇒ If there is a delay in getting the CTPA then give LMWH until the scan is performed.
- If the patient has an allergy to contrast media or renal impairment a **V/Q scan** should be used instead of a CTPA.

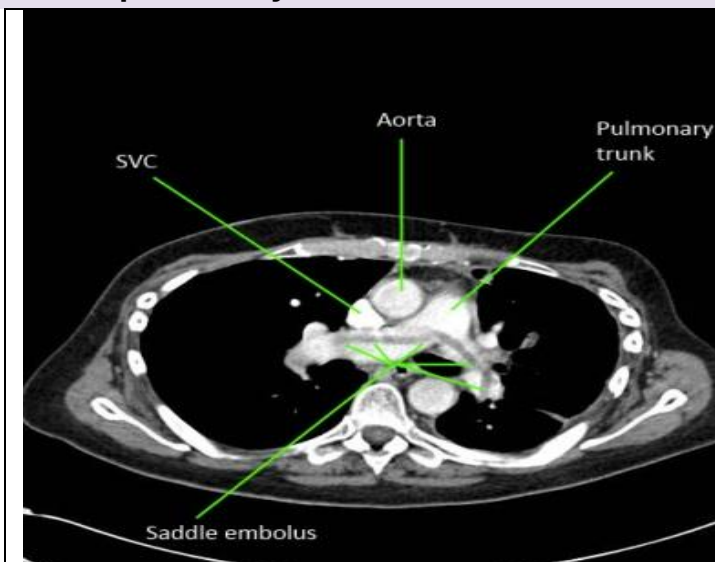
CTPA or V/Q scan?

The consensus view from the British Thoracic Society and NICE guidelines is as follows:

A) Computed tomographic pulmonary angiography (CTPA)

- It is now the recommended **initial lung-imaging modality** for non-massive PE.
- Advantages compared to V/Q scans include:
 - 1) speed, easier to perform out-of-hours,
 - 2) a reduced need for further imaging and the possibility of providing an alternative diagnosis if PE is excluded
 - 3) if the CTPA is negative then patients do not need further investigations or treatment for PE

B) ventilation-perfusion scanning may be used initially if appropriate facilities exist, the chest x-ray is normal, and there is no significant symptomatic concurrent cardiopulmonary disease



Labelled CTPA showing a large saddle embolus



Further CTPA again showing a saddle embolus

Some other points

D-dimers:

- sensitivity = 95-98%, but poor specificity (good -ve)

ECG:

- **S1Q3T3**: the classic ECG changes seen in PE are a large S wave in lead I, a large Q wave in lead III and an inverted T wave in lead III - '**S1Q3T3**'. However this change is seen in no more than 20% of patients
- **RBBB** and **RAD** are also associated with PE
- **sinus tachycardia** may also be seen



ECG from a patient with a PE. Shows a sinus tachycardia and a partial S1Q3T3 - the S wave is not particularly convincing.



ECG of a patient with a PE. It shows some of the ECG features that may be associated with PE (sinus tachycardia, S1, T3 and T wave inversion in the precordial leads). Other features such as the left axis deviation are atypical.

V/Q scan:

- ✓ sensitivity = 98%; specificity = 40% - high negative predictive value, i.e. **if normal virtually excludes PE**
- ✓ other causes of mismatch in V/Q include:
 - 1) old pulmonary embolisms,
 - 2) AV malformations,
 - 3) vasculitis,
 - 4) previous radiotherapy
 - 5) COPD gives matched defects

CTPA:

- ✓ **initial lung-imaging modality**
- ✓ peripheral emboli affecting subsegmental arteries may be missed

Pulmonary angiography:

- ✓ **the gold standard**
- ✓ significant complication rate compared to other investigations

Pulmonary embolism management:

- The NICE guidelines of 2012 provided some clarity on how long patients should be anticoagulated for after a pulmonary embolism (PE). Selected points are listed below.
- **LMWH** or **fondaparinux** should be given initially after a PE is diagnosed.

An exception to this is for:

- ⇒ Patients with a massive PE where **thrombolysis** is being considered.
- ⇒ In such a situation **unfractionated heparin** should be used.

- a vitamin K antagonist (i.e. **warfarin**) should be given within 24 hours of the diagnosis
- the LMWH or fondaparinux should be continued for at least 5 days or until INR is 2.0 or above for at least 24 hours, whichever is longer, i.e. LMWH or fondaparinux is given at the same time as warfarin until the INR is in the therapeutic range
- Warfarin should be continued for at least 3 months. At 3 months, NICE advise that clinicians should 'assess the risks and benefits of extending treatment'
- NICE advice extending warfarin beyond 3 months for patients with unprovoked PE. This essentially means that if there was no obvious cause or provoking factor (surgery, trauma, significant immobility) it may imply the patient has a tendency to thrombosis and should be given treatment longer than the norm of 3 months
- For patients with **active cancer** NICE recommend using LMWH for **6 months???** (**lifelong**) or **till cure of cancer.????**

Thrombolysis:

- Thrombolysis is now recommended as the **first-line treatment** for **massive PE** where there is circulatory failure (e.g. hypotension, acidosis).
- Other invasive approaches should be considered where appropriate facilities exist

Pregnancy: DVT/PE investigation

Guidelines were updated in 2010 by the Royal College of Obstetricians. Key points include:

- 1) chest x-ray should be performed in all patients
- 2) compression duplex Doppler:
 - ⇒ should be performed if the chest x-ray is normal
 - ⇒ this may provide indirect evidence of a pulmonary embolism and negate the need for further radiation exposure
- 3) the decision to perform a V/Q or CTPA should be taken at a local level after discussion with the patient and radiologist

Comparing CTPA to V/Q scanning in pregnancy:

CTPA	V/Q scanning
- CTPA slightly increases the lifetime risk of maternal breast cancer (increased by up to 13.6%, background risk of 1/200 for study population). - Pregnancy makes breast tissue particularly sensitive to the effects of radiation	V/Q scanning carries a slightly increased risk of childhood cancer compared with CTPA (1/280,000 versus less than 1/1,000,000)

D-dimer is of limited use in the investigation of thromboembolism as it often rose in pregnancy.

Oxygen therapy

- The British Thoracic Society published guidelines on emergency oxygen therapy in 2008.
- **The following selected points are taken from the guidelines.**
 - In patients who are critically ill (anaphylaxis, shock etc) oxygen should initially be given via a **reservoir mask at 15 l/min**. **Hypoxia kills**.
 - The BTS guidelines specifically exclude certain conditions where the patient is acutely unwell (e.g. myocardial infarction) but stable.

Oxygen saturation targets:

- 1) acutely ill patients: 94-98%
- 2) patients at risk of hypercapnia (e.g. COPD patients): 88-92%
- 3) oxygen should be reduced in stable patients with satisfactory oxygen saturation

Management of COPD patients:

- 1) prior to availability of blood gases, use a **28% Venturi mask at 4 l/min** and aim for an oxygen saturation of **88-92%** for patients with risk factors for hypercapnia but no prior history of respiratory acidosis
- 2) adjust target range to **94-98%** if the **pCO₂ is normal**

Situations where oxygen therapy **should not** be used routinely if there is no evidence of hypoxia:

- 1) myocardial infarction and acute coronary syndromes
- 2) stroke
- 3) obstetric emergencies
- 4) anxiety-related hyperventilation

Non-invasive ventilation

- The British Thoracic Society (BTS) published guidelines in 2002 on the use of non-invasive ventilation in acute respiratory failure.
- Following these the Royal College of Physicians published guidelines in 2008.

Key indications

- 1) **COPD** with respiratory acidosis **pH 7.25-7.35**
- 2) **type II respiratory failure** secondary to **chest wall deformity, neuromuscular disease** or **obstructive sleep apnoea**
- 3) **cardiogenic pulmonary oedema** unresponsive to CPAP
- 4) **weaning** from tracheal intubation

Recommended initial settings for bi-level pressure support in COPD

- 1) Expiratory Positive Airway Pressure (**EPAP**): **4-5 cm H₂O**
- 2) Inspiratory Positive Airway Pressure (**IPAP**): RCP advocate **10 cm H₂O** whilst BTS suggest **12-15 cm H₂O**
- 3) **back up rate**: **15 breaths/min**
- 4) **back up inspiration: expiration ratio**: **1:3**

Acute exacerbation of COPD (AECOPD) & type II respiratory failure

- The choices are either non-invasive ventilation (NIV) through a full face or nasal mask, or endotracheal intubation (ETI) with ventilation on an ICU.
- In selected patients with type 2 respiratory failure due to AECOPD **NIV** has been shown to **decrease mortality** and **length of hospital stay** over ETI.

However there are **contraindications to NIV**:

- 1) Haemodynamically unstable
- 2) Confusion / impaired consciousness
- 3) Vomiting
- 4) Inability to protect airway
- 5) Fixed obstruction of the upper airway
- 6) Facial burns/traums, and
- 7) Undrained pneumothorax.

It should be noted however NIV may be used despite many of these contraindications if NIV is to be the ceiling of treatment.

The criteria for LTOT are PaO₂ less than 7.3 kPa (55 mmHg) with or without hypercapnia or PaO₂ less than 8.0 kPa (60 mmHg) if there is evidence of pulmonary hypertension/cor pulmonale/polycythaemia. See [COPD](#) for more details

LTOT and smoking cessation are currently the only interventions in COPD that have been shown to prolong life.

Post-extubation stridor (PES):

- A frequent complication of intubation, occurring in 2-16% of cases.
- It is caused by laryngeal oedema that results from damage to the mucosa of the larynx.
- Mucosal damage is caused by pressure and ischaemia resulting in an inflammatory response.
- Laryngeal oedema, in severe cases, can lead to acute respiratory compromise necessitating emergency reintubation.
- Female gender is a risk factor for both laryngeal oedema and PES.
- This predisposition has been hypothesised to be due to the female mucous membrane being less resistant to trauma and thinner than that in men.

Other risk factors include:

- Female gender
- Intubation >36 hours
- Excessive cuff pressure
- Large tube size, and
- Tracheal infection.

Age and asthma are not known risk factors for PES.

- The misplacement of a nasogastric tube (NG) in the lungs and proceeding to 'enteral feeding' is a potential cause of death.
- The National Patient Safety Agency (NPSA) and Medical Protection Society (MPS) have highlighted the potential for catastrophe and suggested methods of preventing such 'never-events'.
- Between 2005 and March 2011 the NPSA were notified of 21 deaths and 79 cases of harm secondary to a misplaced NG tubes.
- The first line test to confirm correct placement is to test the gastric aspirate with **pH indicator paper**.
- If the **pH is between 1- 5.5** then this is confirmatory evidence of correct placement.
- If there is any doubt, then an appropriately interpreted chest x ray is a second line investigation.
- There is no place for the use of non-quantitative litmus paper or the 'whoosh' and 'blow' tests, as these methods are notoriously unreliable.
- New devices that track the passage of a magnetised tip of a nasogastric past the diaphragm are currently being assessed. Their role in confirming correct placement is not established yet.

Rheumatoid arthritis: respiratory manifestations

- 1) pulmonary fibrosis
- 2) pulmonary nodules
- 3) Caplan's syndrome - massive fibrotic nodules with occupational coal dust exposure
- 4) bronchiolitis obliterans
- 5) pleurisy
- 6) pleural effusion (the commonest)
- 7) bronchiectasis (especially non smokers)
- 8) complications of drug therapy e.g. methotrexate pneumonitis, sulfasalazine, gold
- 9) infection (possibly atypical) secondary to immunosuppression

Respiratory acidosis

Respiratory acidosis may be caused by a number of conditions

- COPD
- decompensation in other respiratory conditions e.g. life-threatening asthma / pulmonary oedema
- sedative drugs: benzodiazepines, opiate overdose

Respiratory alkalosis

Common causes

- anxiety leading to hyperventilation
- pulmonary embolism
- salicylate poisoning*
- CNS disorders: stroke, subarachnoid haemorrhage, encephalitis
- altitude
- pregnancy

*salicylate overdose leads to a mixed respiratory alkalosis and metabolic acidosis. Early stimulation of the respiratory centre leads to a respiratory alkalosis whilst later the direct acid effects of salicylates (combined with acute renal failure) may lead to an acidosis

An 82-year-old man presents with weight loss (5 kg) and a hoarse voice of two months duration.

His chest radiograph is shown below.



The chest X ray shows left upper lobar consolidation; the history of hoarseness implies involvement of the recurrent laryngeal nerve - most likely due to invasion by tumour. Upper lobar malignancies involving the superior pulmonary sulcus can destroy surrounding structures leading to a characteristic clinical pattern - Pancoast's syndrome. The syndrome consists of pain in a C8-T2 distribution (caused by infiltration of these nerves) often accompanied by radiological evidence of destruction of the first and second ribs. Horner's syndrome frequently co-exists due to infiltration of the sympathetic trunk. Horner's syndrome consists of enophthalmos, ptosis, miosis and ipsilateral loss of the ability to sweat.